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NEWS 2	OCT 02	CA/CAplus enhanced with pre-1907 records from Chemisches Zentralblatt
NEWS 3	OCT 19	BEILSTEIN updated with new compounds
NEWS 4	NOV 15	Derwent Indian patent publication number format enhanced
NEWS 5	NOV 19	WPIX enhanced with XML display format
NEWS 6	NOV 30	ICSD reloaded with enhancements
NEWS 7	DEC 04	LINPADOCDB now available on STN
NEWS 8	DEC 14	BEILSTEIN pricing structure to change
NEWS 9	DEC 17	USPATOLD added to additional database clusters
NEWS 10	DEC 17	IMSDRUGCONF removed from database clusters and STN
NEWS 11	DEC 17	DGENE now includes more than 10 million sequences
NEWS 12	DEC 17	TOXCENTER enhanced with 2008 MeSH vocabulary in MEDLINE segment
NEWS 13	DEC 17	MEDLINE and LMEDLINE updated with 2008 MeSH vocabulary
NEWS 14	DEC 17	CA/CAplus enhanced with new custom IPC display formats
NEWS 15	DEC 17	STN Viewer enhanced with full-text patent content from USPATOLD
NEWS 16	JAN 02	STN pricing information for 2008 now available
NEWS 17	JAN 16	CAS patent coverage enhanced to include exemplified prophetic substances
NEWS 18	JAN 28	USPATFULL, USPAT2, and USPATOLD enhanced with new custom IPC display formats
NEWS 19	JAN 28	MARPAT searching enhanced
NEWS 20	JAN 28	USGENE now provides USPTO sequence data within 3 days of publication
NEWS 21	JAN 28	TOXCENTER enhanced with reloaded MEDLINE segment
NEWS 22	JAN 28	MEDLINE and LMEDLINE reloaded with enhancements
NEWS 23	FEB 08	STN Express, Version 8.3, now available
NEWS 24	FEB 20	PCI now available as a replacement to DPCI
NEWS 25	FEB 25	IFIREF reloaded with enhancements
NEWS 26	FEB 25	IMSPRODUCT reloaded with enhancements
NEWS 27	FEB 29	WPINDEX/WPIDS/WPIX enhanced with ECLA and current U.S. National Patent Classification

NEWS EXPRESS FEBRUARY 08 CURRENT WINDOWS VERSION IS V8.3,
AND CURRENT DISCOVER FILE IS DATED 20 FEBRUARY 2008

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NEWS IPC8	For general information regarding STN implementation of IPC 8

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* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 15:36:12 ON 18 MAR 2008

=> file medline
COST IN U.S. DOLLARS   SINCE FILE   TOTAL
                                                         ENTRY   SESSION
FULL ESTIMATED COST   1.47   1.47

FILE 'MEDLINE' ENTERED AT 15:40:16 ON 18 MAR 2008

 FILE LAST UPDATED: 15 Mar 2008 (20080315/UP). FILE COVERS 1949 TO DATE.

  MEDLINE has been updated with the National Library of Medicine's
  revised 2008 MeSH terms. See HELP RLOAD for details.

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

=> s stearoyl-coa desaturase
          1936 STEAROYL
         36924 COA
           811 COAS
         37074 COA
                 (COA OR COAS)
          2952 DESATURASE
          2426 DESATURASES
          4066 DESATURASE
                 (DESATURASE OR DESATURASES)
L1   697 STEAROYL-COA DESATURASE
                 (STEAROYL(W)COA(W)DESATURASE)

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L2   21 L1 AND REVIEW

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L3   2 L2 AND 2003/PY

=> d 1-2 ibib abs

L3   ANSWER 1 OF 2   MEDLINE on STN
ACCESSION NUMBER: 2003311563   MEDLINE
DOCUMENT NUMBER: PubMed ID: 12840656
TITLE: Recent insights into stearoyl-CoA
                    desaturase-1.
AUTHOR: Ntambi James M; Miyazaki Makoto
CORPORATE SOURCE: Departments of Biochemistry and Nutritional Sciences,
                    University of Wisconsin, Madison, Wisconsin 53706, USA..
                    ntambi@biochem.wisc.edu
CONTRACT NUMBER: R0162388

SOURCE: Current opinion in lipidology, (2003 Jun) Vol. 14, No. 3, pp. 255-61. Ref: 81
Journal code: 9010000. ISSN: 0957-9672.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200402
ENTRY DATE: Entered STN: 4 Jul 2003
Last Updated on STN: 6 Feb 2004
Entered Medline: 5 Feb 2004

AB PURPOSE OF REVIEW: Stearoyl-Coenzyme A (CoA) desaturase is a central lipogenic enzyme catalyzing the synthesis of monounsaturated fatty acids - mainly oleate (C(18:1)). Oleate is the most abundant monounsaturated fatty acid in dietary fat and is therefore readily available. Why, then, is stearoyl-CoA desaturase a highly regulated enzyme? This review summarizes the recent and timely advances concerning the important role of stearoyl-CoA desaturase in metabolism. RECENT FINDINGS: Recent findings using mice that have a naturally occurring mutation in the SCD1 gene isoform as well as a mouse model with a targeted disruption of the stearoyl-CoA desaturase gene-1 (SCD1-/-) have revealed the role of de-novo synthesized oleate and thus the physiological importance of SCD1 expression. In the highlighted references, it is shown that the SCD1-/- mice have reduced body adiposity, increased insulin sensitivity, and are resistant to diet-induced obesity. The expression of several genes of lipid oxidation is upregulated, whereas lipid synthesis genes are downregulated. SCD1 was also found to be a component of the novel metabolic response to the hormone leptin. SUMMARY: SCD1, therefore, appears to be an important metabolic control point, and inhibition of its expression could be of benefit for the treatment of obesity, diabetes and other metabolic diseases.

L3 ANSWER 2 OF 2 MEDLINE on STN
ACCESSION NUMBER: 2003031722 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12538075
TITLE: Role of stearoyl-coenzyme A desaturase in lipid metabolism.
AUTHOR: Miyazaki Makoto; Ntambi James M
CORPORATE SOURCE: Department of Biochemistry, University of Wisconsin-Madison, 433 Babcock Drive, WI 53706, USA.
SOURCE: Prostaglandins, leukotrienes, and essential fatty acids, (2003 Feb) Vol. 68, No. 2, pp. 113-21. Ref: 122
Journal code: 8802730. ISSN: 0952-3278.
PUB. COUNTRY: Scotland: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200309
ENTRY DATE: Entered STN: 23 Jan 2003
Last Updated on STN: 28 Sep 2003
Entered Medline: 26 Sep 2003

AB Stearoyl-CoA desaturase (SCD) (EC 1.14.99.5) is an endoplasmic reticulum-bound enzyme that catalyzes the delta9-cis desaturation of saturated fatty acyl-CoAs, the preferred substrates being palmitoyl- and stearoyl-CoA, which are converted to palmitoleoyl- and oleoyl-CoA, respectively. These monounsaturated fatty acids are used as substrates for the synthesis of triglycerides, wax esters, cholesteryl

esters and membrane phospholipids. The saturated to monounsaturated fatty acid ratio affects membrane phospholipid composition and alteration in this ratio has been implicated in a variety of disease states including cardiovascular disease, obesity, diabetes, neurological disease, skin disorders and cancer. Thus, the expression of SCD is of physiological importance in normal and disease states. Several mammalian SCD genes have been cloned. A single human, three mouse and two rat are the best characterized SCD genes. The physiological role of each SCD isoform and the reason for having three or more SCD gene isoforms in the rodent genome are currently unknown. A clue as to the physiological role of the SCD, at least SCD1 gene and its endogenous products came from recent studies of asebia mouse strains that have a natural mutation in the SCD1 gene and a mouse model with a targeted disruption of the SCD1 gene. In this review we discuss our current understanding of the physiological role of SCD in lipid synthesis and metabolism.

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NEWS 11	FEB 25	IFIREF reloaded with enhancements
NEWS 12	FEB 25	IMSPRODUCT reloaded with enhancements
NEWS 13	FEB 29	WPINDEX/WPIDS/WPIX enhanced with ECLA and current U.S. National Patent Classification
NEWS 14	MAR 31	IFICDB, IFIPAT, and IFIUDB enhanced with new custom IPC display formats
NEWS 15	MAR 31	CAS REGISTRY enhanced with additional experimental spectra
NEWS 16	MAR 31	CA/CAplus and CASREACT patent number format for U.S. applications updated
NEWS 17	MAR 31	LPCI now available as a replacement to LDPCI
NEWS 18	MAR 31	EMBASE, EMBAL, and LEMBASE reloaded with enhancements
NEWS 19	APR 04	STN AnaVist, Version 1, to be discontinued
NEWS 20	APR 15	WPIDS, WPINDEX, and WPIX enhanced with new predefined hit display formats
NEWS 21	APR 28	EMBASE Controlled Term thesaurus enhanced

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 NEWS 22  APR 28  IMSRESEARCH reloaded with enhancements

 NEWS EXPRESS FEBRUARY 08 CURRENT WINDOWS VERSION IS V8.3,
              AND CURRENT DISCOVER FILE IS DATED 20 FEBRUARY 2008

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FILE 'HOME' ENTERED AT 10:25:09 ON 20 MAY 2008

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DICTIONARY FILE UPDATES:  19 MAY 2008  HIGHEST RN 1021481-05-9

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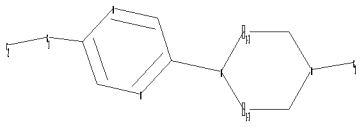

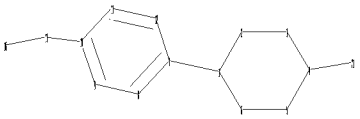

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13 16 21
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12
chain bonds :
1-7 4-21 10-13 13-16
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12
exact/norm bonds :
1-2 1-6 1-7 2-3 3-4 4-5 4-21 5-6 10-13 13-16
normalized bonds :
7-8 7-12 8-9 9-10 10-11 11-12

G1:C,N

G2:C,O,N

G3:C,S

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:CLASS 16:CLASS 21:CLASS

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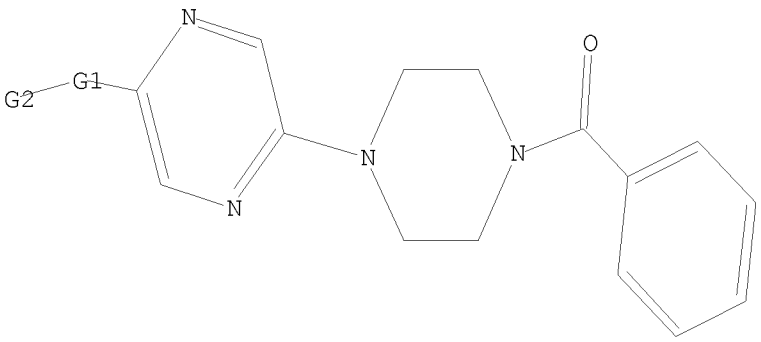
L1 STR



G1 C,N

G2 C,O,N

Structure attributes must be viewed using STN Express query preparation.

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100.0% PROCESSED       42 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          452 TO     1228
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SEARCH TIME: 00.00.01

L3           13 SEA SSS FUL L1

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                                                         ENTRY    SESSION
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=> s l3
L4 3 L3

=> d 1-3 ibib abs hitstr

L4 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:141044 CAPLUS
DOCUMENT NUMBER: 142:240465
TITLE: Preparation of alkoxybenzoylpiperazines as inhibitors of glycine transporter 1 (GlyT-1)
INVENTOR(S): Jolidon, Synese; Narquizian, Robert; Nettekoven, Matthias Heinrich; Norcross, Roger David; Pinard, Emmanuel; Stalder, Henri
PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
SOURCE: PCT Int. Appl., 241 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005014563	A1	20050217	WO 2004-EP8633	20040802
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004263306	A2	20050217	AU 2004-263306	20040802
AU 2004263306	A1	20050217		
CA 2534675	A1	20050217	CA 2004-2534675	20040802
EP 1656361	A1	20060517	EP 2004-763703	20040802
EP 1656361	B1	20080102		
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BR 2004013497	A	20061017	BR 2004-13497	20040802
CN 1867554	A	20061122	CN 2004-80029755	20040802
JP 2007501820	T	20070201	JP 2006-522944	20040802
AT 382611	T	20080115	AT 2004-763703	20040802
ES 2297458	T3	20080501	ES 2004-763703	20040802
US 20050209241	A1	20050922	US 2004-911359	20040804
US 7319099	B2	20080115		
TW 289556	B	20071111	TW 2004-93123828	20040809

NO 2006000541	A	20060308	NO 2006-541		20060202
KR 774622	B1	20071108	KR 2006-702786		20060209
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IN 2006CN00506	A	20070706	IN 2006-CN506		20060210
PRIORITY APPLN. INFO.:			EP 2003-17614	A	20030811
			WO 2004-EP8633	W	20040802

OTHER SOURCE(S): MARPAT 142:240465

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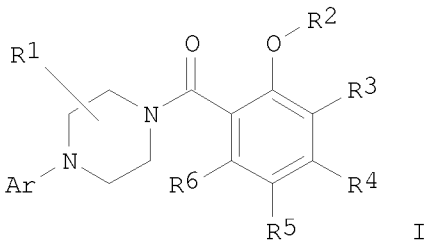

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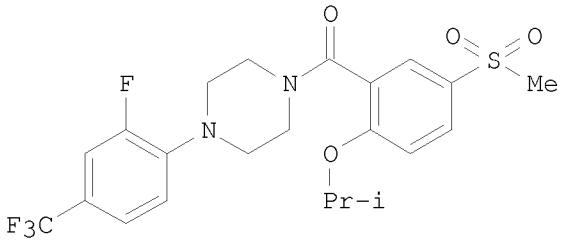


II

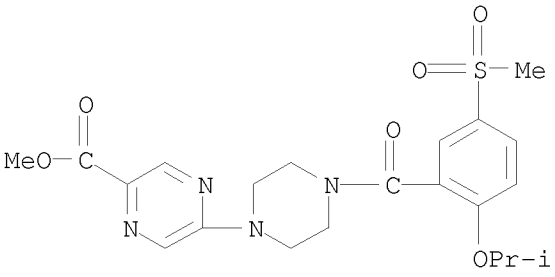
AB Title compds. I [wherein Ar = (un)substituted aryl or 6-membered heteroaryl; R1 = H, alkyl; R2 = H, alkyl, alkenyl, (un)substituted cycloalkyl, etc.; R3, R4, R6 = independently H, OH, halo, cyclo/alkyl, alkoxy; R5 = NO2, CN, CHO and derivs., SO2R10; R10 = (un)substituted alkyl; and their pharmaceutically acceptable acid addition salts, with the exception of certain compds.] were prepared as glycine transporter 1 (GlyT-1) inhibitors. For instance, reacting 2-isopropoxy-5-methylsulfonylbenzoic acid (preparation given) with 1-(2-fluoro-4-trifluoromethylphenyl)piperazine gave piperazine II. I showed an IC50 (μM) at GlyT-1 in the range of 0.006-5.0. Preferred I displayed an IC50 (μM) at GlyT-1 in the range of 0.006-0.05. Thus, I are useful in the treatment of illnesses based on the glycine uptake inhibitor, such as psychoses, pain, neurodegenerative disfunction in memory and learning, schizophrenia, dementia and other diseases in which cognitive processes are impaired, such as attention deficit disorders or Alzheimer's disease.

IT 845612-79-5P, 4-(2-Isopropoxy-5-methylsulfonylbenzoyl)-3,4,5,6-Tetrahydro-2H-[1,2']bipyrazinyl-5'-carboxylic acid methyl ester
845612-80-8P, 4-(2-Isobutoxy-5-methylsulfonylbenzoyl)-3,4,5,6-Tetrahydro-2H-[1,2']bipyrazinyl-5'-carboxylic acid methyl ester
845612-83-1P, 4-(2-Isobutoxy-5-methylsulfonylbenzoyl)-3,4,5,6-Tetrahydro-2H-[1,2']bipyrazinyl-5'-carboxamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of alkoxybenzoylpiperazines as inhibitors of

glycine transporter 1 (GlyT-1))

RN 845612-79-5 CAPLUS

CN 2-Pyrazinecarboxylic acid, 5-[4-[2-(1-methylethoxy)-5-(methylsulfonyl)benzoyl]-1-piperazinyl]-, methyl ester (CA INDEX NAME)



RN 845612-80-8 CAPLUS

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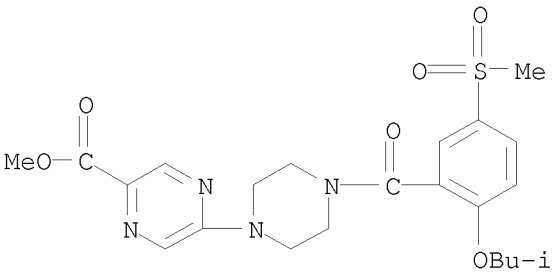

RN 845612-83-1 CAPLUS

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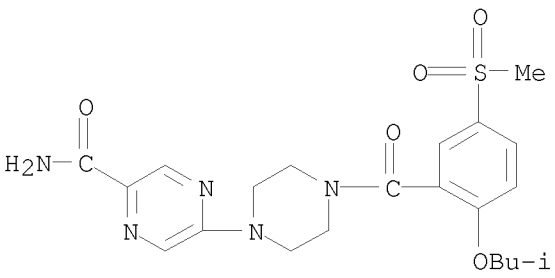

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L4 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:120716 CAPLUS

DOCUMENT NUMBER: 142:219312

TITLE: Preparation of piperazine derivatives as stearoyl-CoA desaturase inhibitors for the treatment of diabetes and other diseases

INVENTOR(S): Sviridov, Serguei; Kodumuru, Vishnumurthy; Liu,

Shifeng; Abreo, Melwyn; Winther, Michael D.; Gschwend, Heinz W.; Kamboj, Rajender; Sun, Shaoyi; Holladay, Mark W.; Li, Wenbao; Tu, Chi

PATENT ASSIGNEE(S): Xenon Pharmaceuticals Inc., Can.

SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2005011657	A2	20050210	WO 2004-US24658		20040729
WO 2005011657	A3	20050324			
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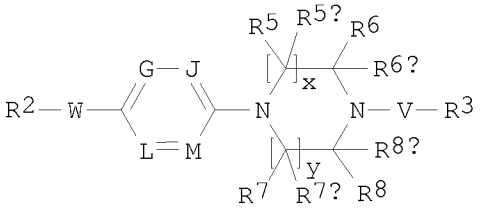
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2004261268	A1	20050210	AU 2004-261268		20040729
CA 2533901	A1	20050210	CA 2004-2533901		20040729
EP 1651620	A2	20060503	EP 2004-779656		20040729
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR					
BR 2004012348	A	20060905	BR 2004-12348		20040729
CN 1829701	A	20060906	CN 2004-80021942		20040729
JP 2007500720	T	20070118	JP 2006-522096		20040729
US 20060009459	A1	20060112	US 2005-55034		20050209
MX 2006PA01206	A	20060920	MX 2006-PA1206		20060130
US 20060252767	A1	20061109	US 2006-567009		20060130
NO 2006000971	A	20060502	NO 2006-971		20060228
PRIORITY APPLN. INFO.:			US 2003-491095P	P	20030730
			US 2004-546786P	P	20040223
			US 2004-546815P	P	20040223
			US 2004-546820P	P	20040223
			US 2004-546898P	P	20040223
			US 2004-546934P	P	20040223
			US 2004-553403P	P	20040316
			US 2004-553404P	P	20040316
			US 2004-553416P	P	20040316
			US 2004-553446P	P	20040316
			US 2004-553491P	P	20040316
			US 2004-901563	A2	20040729
			WO 2004-US24658	W	20040729

OTHER SOURCE(S): CASREACT 142:219312; MARPAT 142:219312

GI



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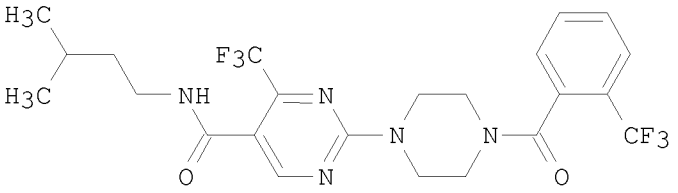


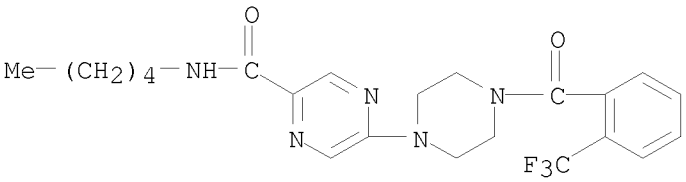
II

AB Title compds. I [wherein x, y = 1-3; W = N(R1)C(O), C(O)N(R1), O, S or S(O)2; V = C(O/S) or C(R10)H; G, J, L, M = N or C(R4); R1 = H or (un)substituted alkyl; R2, R3 = (un)substituted alk(en)yl, (hetero)aryl or heterocyclyl; R4 = H, F, Me, OMe or cyano; R5, R5a, R6, R6a, R7, R7a, R8, R8a, R10 = H or alkyl; etc., and stereoisomers, enantiomers or tautomers, pharmaceutically acceptable salts, pharmaceutical compns. or prodrugs thereof] were prepared as stearoyl-CoA desaturase (SCD) inhibitors. For example, amidation of 2-chloro-4-trifluoromethylpyrimidine-5-carbonyl chloride with 3-methylbutylamine (70% yield) followed by substitution with piperazine gave a monofunctionlized piperazine (86% yield). This compound underwent benzoylation with 2-trifluoromethylbenzoyl chloride to afford piperazinylpyrimidine II (76% yield). I and their pharmaceutical compns. are useful in the treatment or prevention of various human diseases, including those mediated by stearoyl-CoA desaturase (SCD) enzymes, especially diseases related to elevated lipid levels, cardiovascular disease, diabetes, obesity, metabolic syndrome and the like.

IT 842170-26-7P 842170-28-9P 842170-29-0P
842170-30-3P 842170-31-4P 842170-37-0P
842170-38-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(inhibitor; preparation of piperazine derivs. as stearoyl-CoA desaturase inhibitors)

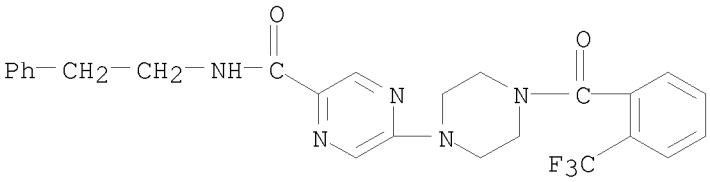
RN 842170-26-7 CAPLUS

CN 2-Pyrazinecarboxamide, N-pentyl-5-[4-[2-(trifluoromethyl)benzoyl]-1-piperazinyl]- (CA INDEX NAME)

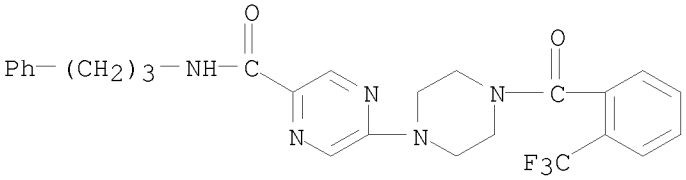


RN 842170-28-9 CAPLUS

CN 2-Pyrazinecarboxamide, N-(2-phenylethyl)-5-[4-[2-(trifluoromethyl)benzoyl]-1-piperazinyl]- (CA INDEX NAME)



RN 842170-29-0 CAPLUS
CN 2-Pyrazinecarboxamide, N-(3-phenylpropyl)-5-[4-[2-(trifluoromethyl)benzoyl]-1-piperazinyl]- (CA INDEX NAME)



RN 842170-30-3 CAPLUS
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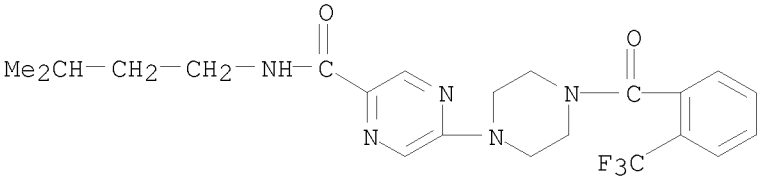
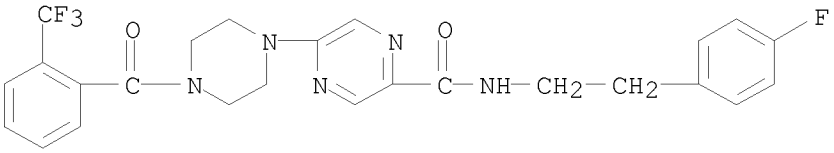
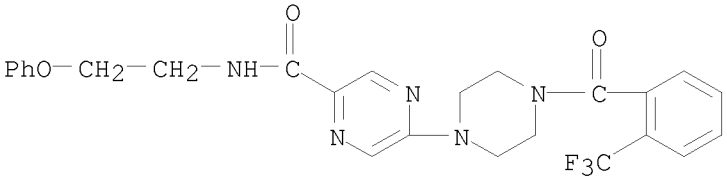


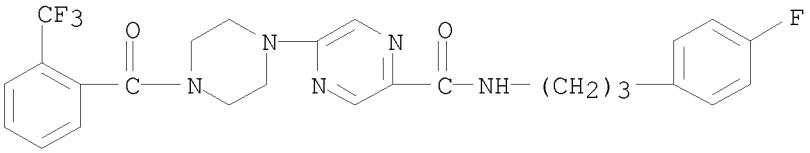
RN 842170-31-4 CAPLUS
CN 2-Pyrazinecarboxamide, N-[2-(4-fluorophenyl)ethyl]-5-[4-[2-(trifluoromethyl)benzoyl]-1-piperazinyl]- (CA INDEX NAME)



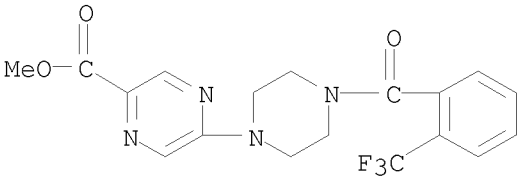
RN 842170-37-0 CAPLUS
CN 2-Pyrazinecarboxamide, N-(2-phenoxyethyl)-5-[4-[2-(trifluoromethyl)benzoyl]-1-piperazinyl]- (CA INDEX NAME)



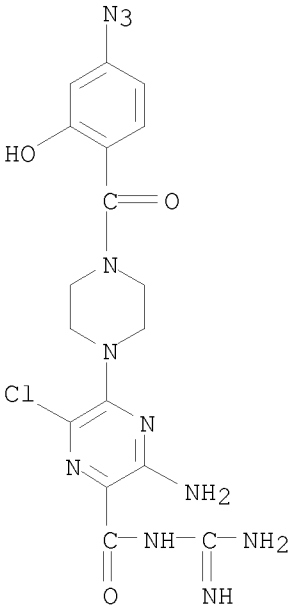
RN 842170-38-1 CAPLUS
CN 2-Pyrazinecarboxamide, N-[3-(4-fluorophenyl)propyl]-5-[4-[2-(trifluoromethyl)benzoyl]-1-piperazinyl]- (CA INDEX NAME)



IT 842170-27-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of piperazine derivs. as stearoyl-CoA desaturase inhibitors)
RN 842170-27-8 CAPLUS
CN 2-Pyrazinecarboxylic acid, 5-[4-[2-(trifluoromethyl)benzoyl]-1-piperazinyl]-, methyl ester (CA INDEX NAME)

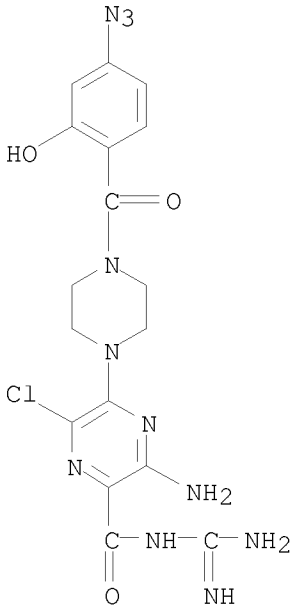


L4 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1990:402710 CAPLUS
DOCUMENT NUMBER: 113:2710
ORIGINAL REFERENCE NO.: 113:551a,554a
TITLE: Photoactivatable probe for the sodium/hydrogen ion exchanger cross-links a 66-kDa renal brush border membrane protein
AUTHOR(S): Ross, Willie; Bertrand, William; Morrison, Aubrey
CORPORATE SOURCE: Sch. Med., Washington Univ., St. Louis, MO, 63110, USA
SOURCE: Journal of Biological Chemistry (1990), 265(10), 5341-4
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Earlier studies on LLC-PK1 cells have demonstrated 2 pharmacol. distinct Na+/H+ exchangers in renal epithelia. In addition, the cDNA clone for the human Na+/H+ antiporter which is growth factor activatable has been isolated and expressed (Sardet, C., et al., 1989). Here the synthesis of an amiloride analog that can be photoactivated and labeled with 125I is reported. This analog covalently crosslinks a 66-kDa protein of bovine renal brush border membranes. A rabbit polyclonal antibody that was directed against a 20-amino acid peptide of the cytoplasmic domain of its human Na+/H+ antiporter also gives a pos. Western against 66-kDa protein of bovine brush border membranes. Thus, the photoactive probe may be helpful in the isolation and purification of the brush border Na+/H+ exchanger.
IT 127628-92-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and radioiodonation of)
RN 127628-92-6 CAPLUS
CN Pyrazinecarboxamide, 3-amino-N-(aminoiminomethyl)-5-[4-(4-azido-2-hydroxybenzoyl)-1-piperazinyl]-6-chloro- (9CI) (CA INDEX NAME)



IT 127513-40-0
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of, as photoactivable probe for sodium-hydroxy ion exchanger)
RN 127513-40-0 CAPLUS
CN Pyrazinecarboxamide, 3-amino-N-(aminoiminomethyl)-5-[4-[4-azido-2-hydroxy-3(or 5)-(iodo-125I)benzoyl]-1-piperazinyl]-6-chloro- (9CI) (CA INDEX NAME)

PAGE 1-A



D1— ^{125}I

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	24.03	202.60

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-2.40	-2.40

FILE 'REGISTRY' ENTERED AT 10:35:14 ON 20 MAY 2008

Property values tagged with IC are from the ZIC/VINITI data file
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STRUCTURE FILE UPDATES: 19 MAY 2008 HIGHEST RN 1021481-05-9
DICTIONARY FILE UPDATES: 19 MAY 2008 HIGHEST RN 1021481-05-9

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REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

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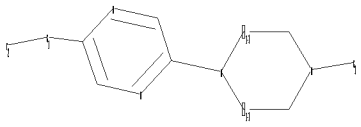
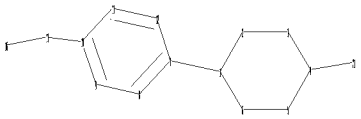
Uploading C:\Program Files\Stnexp\Queries\10567009.str





chain nodes :
13 16 21
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12
chain bonds :
1-7 4-21 10-13 13-16
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12
exact/norm bonds :
1-2 1-6 1-7 2-3 3-4 4-5 4-21 5-6 10-13 13-16
normalized bonds :
7-8 7-12 8-9 9-10 10-11 11-12

G1:C,N

G2:C,O,N

G3:C,S

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:CLASS 16:CLASS 21:CLASS

L5 STRUCTURE UPLOADED

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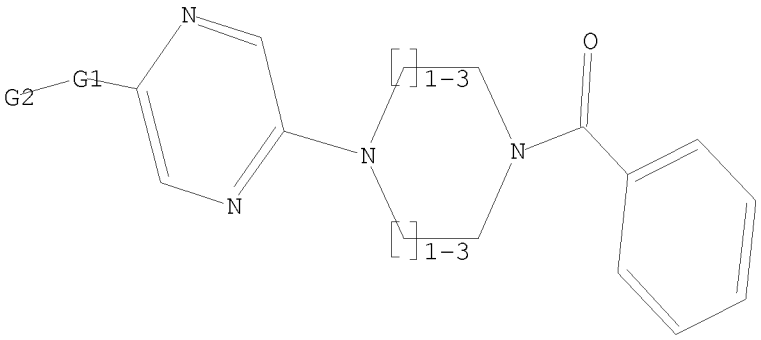
L5 HAS NO ANSWERS
L5 STR



G1 C,N

G2 C,O,N

Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SCREEN SEARCH COMPLETED -       45 TO ITERATE

100.0% PROCESSED       45 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          498 TO     1302
PROJECTED ANSWERS:               0 TO        0

L6            0 SEA SSS SAM L5

=> s l5 sss full
FULL SEARCH INITIATED 10:35:38 FILE 'REGISTRY'
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100.0% PROCESSED      985 ITERATIONS                               13 ANSWERS
SEARCH TIME: 00.00.01

L7           13 SEA SSS FUL L5

=> d his

     (FILE 'HOME' ENTERED AT 10:25:09 ON 20 MAY 2008)

     FILE 'REGISTRY' ENTERED AT 10:25:20 ON 20 MAY 2008
L1              STRUCTURE UPLOADED
L2            0 S L1
L3           13 S L1 SSS FULL

     FILE 'CAPLUS' ENTERED AT 10:25:47 ON 20 MAY 2008
L4            3 S L3

     FILE 'REGISTRY' ENTERED AT 10:35:14 ON 20 MAY 2008
L5              STRUCTURE UPLOADED
L6            0 S L5
L7           13 S L5 SSS FULL
```

```
=> s l7 not l3
L8            0 L7 NOT L3

=> log hold
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                      ENTRY    SESSION
FULL ESTIMATED COST                                  178.36     380.96

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                      ENTRY    SESSION
CA SUBSCRIBER PRICE                                    0.00      -2.40

 SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 10:35:51 ON 20 MAY 2008

Connecting via Winsock to STN



Welcome to STN International!  Enter x:x

LOGINID:ssspta1623zct

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2


* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *

 NEWS  1          Web Page for STN Seminar Schedule - N. America
 NEWS  2  JAN 02  STN pricing information for 2008 now available
 NEWS  3  JAN 16  CAS patent coverage enhanced to include exemplified
                  prophetic substances
 NEWS  4  JAN 28  USPATFULL, USPAT2, and USPATOLD enhanced with new
                  custom IPC display formats
 NEWS  5  JAN 28  MARPAT searching enhanced
 NEWS  6  JAN 28  USGENE now provides USPTO sequence data within 3 days
                  of publication
 NEWS  7  JAN 28  TOXCENTER enhanced with reloaded MEDLINE segment
 NEWS  8  JAN 28  MEDLINE and LMEDLINE reloaded with enhancements
 NEWS  9  FEB 08  STN Express, Version 8.3, now available
 NEWS 10  FEB 20  PCI now available as a replacement to DPCI
 NEWS 11  FEB 25  IFIREF reloaded with enhancements
 NEWS 12  FEB 25  IMSPRODUCT reloaded with enhancements
 NEWS 13  FEB 29  WPINDEX/WPIDS/WPIX enhanced with ECLA and current
                  U.S. National Patent Classification
 NEWS 14  MAR 31  IFICDB, IFIPAT, and IFIUDB enhanced with new custom
                  IPC display formats
 NEWS 15  MAR 31  CAS REGISTRY enhanced with additional experimental
                  spectra
 NEWS 16  MAR 31  CA/CAplus and CASREACT patent number format for U.S.
                  applications updated
 NEWS 17  MAR 31  LPCI now available as a replacement to LDPCI
 NEWS 18  MAR 31  EMBASE, EMBAL, and LEMBASE reloaded with enhancements
 NEWS 19  APR 04  STN AnaVist, Version 1, to be discontinued
 NEWS 20  APR 15  WPIDS, WPINDEX, and WPIX enhanced with new
                  predefined hit display formats
 NEWS 21  APR 28  EMBASE Controlled Term thesaurus enhanced
 NEWS 22  APR 28  IMSRESEARCH reloaded with enhancements

 NEWS EXPRESS FEBRUARY 08 CURRENT WINDOWS VERSION IS V8.3,
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AND CURRENT DISCOVER FILE IS DATED 20 FEBRUARY 2008

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* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 12:59:50 ON 20 MAY 2008

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	1.05	1.05

FILE 'REGISTRY' ENTERED AT 13:02:47 ON 20 MAY 2008
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STRUCTURE FILE UPDATES: 19 MAY 2008 HIGHEST RN 1021481-05-9
DICTIONARY FILE UPDATES: 19 MAY 2008 HIGHEST RN 1021481-05-9

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http://www.cas.org/support/stngen/stndoc/properties.html

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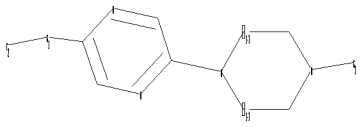
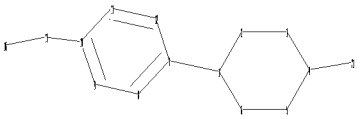




chain nodes :
13 16 21
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12
chain bonds :
1-7 4-21 10-13 13-16
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12
exact/norm bonds :
1-2 1-6 1-7 2-3 3-4 4-5 4-21 5-6 10-13 13-16
normalized bonds :
7-8 7-12 8-9 9-10 10-11 11-12

G1:C,N

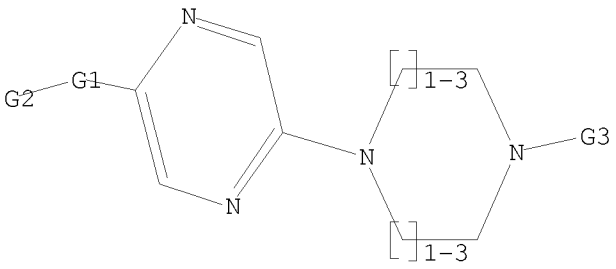
G2:C,O,N

G3:C,S

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:CLASS 16:CLASS 21:CLASS

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



G1 C,N

G2 C,O,N

G3 C,S

Structure attributes must be viewed using STN Express query preparation.

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=> s l1
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SAMPLE SCREEN SEARCH COMPLETED -      437 TO ITERATE

100.0% PROCESSED      437 ITERATIONS                              18 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:         7486 TO     9994
PROJECTED ANSWERS:             106 TO      614

L2           18 SEA SSS SAM L1

=> s l1 sss full
FULL SEARCH INITIATED 13:03:20 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -     9062 TO ITERATE

100.0% PROCESSED     9062 ITERATIONS                             366 ANSWERS
SEARCH TIME: 00.00.01

L3          366 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                               178.36     179.41

FILE 'CAPLUS' ENTERED AT 13:03:28 ON 20 MAY 2008
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FILE COVERS 1907 - 20 May 2008 VOL 148 ISS 21
FILE LAST UPDATED: 19 May 2008 (20080519/ED)

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They are available for your review at:

http://www.cas.org/legal/infopolicy.html

=> s l2
L4   10 L2

=> s l3
L5   41 L3

=> d 1-5

L5   ANSWER 1 OF 41 CAPLUS COPYRIGHT 2008 ACS on STN
AN   2008:43041 CAPLUS
DN   148:144799
TI   Piperazines as P2X7 antagonists and their preparation and use in the
     treatment of diseases
IN   Betschmann, Patrick; Carroll, William A.; Ericsson, Anna M.; Fix-Stenzel,
     Shannon R.; Friedman, Michael; Hirst, Gavin C.; Josephsohn, Nathan S.; Li,
     Biqin; Perez-Medrano, Arturo; Morytko, Michael J.; Rafferty, Paul; Chen,
     Haipeng
PA   Abbott Laboratories, USA
SO   PCT Int. Appl., 328pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2008005368	A2	20080110	WO 2007-US15192	20070629
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	US 20080076924	A1	20080327	US 2007-824441	20070629
PRAI	US 2006-818263P	P	20060630		
OS	MARPAT 148:144799				

L5   ANSWER 2 OF 41 CAPLUS COPYRIGHT 2008 ACS on STN
AN   2007:1204767 CAPLUS
DN   147:502388
TI   Preparation of piperazine derivatives as hepatitis C virus (HCV)
     polymerase inhibitors
IN   Abe, Hiroyuki; Tanaka, Masahiro; Sugimoto, Kazuyuki; Suma, Akira; Yokota,
     Masahiro; Shiozaki, Makoto; Iio, Kiyosei; Ueyama, Kazuhito; Motoda, Dai;
     Noguchi, Toru; Adachi, Tsuyoshi; Tsuruha, Junichiro; Doi, Satoki
PA   Japan Tobacco Inc., Japan
SO   PCT Int. Appl., 1027pp.

CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007119889	A1	20071025	WO 2007-JP58901	20070418
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 20080081818	A1	20080403	US 2007-736064	20070417
PRAI JP 2006-115008	A	20060418		
US 2006-796565P	P	20060501		

OS MARPAT 147:502388
RE.CNT 73 THERE ARE 73 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 41 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2007:730889 CAPLUS
DN 147:166204
TI Substituted isoquinoline-1,3(2H,4H)-diones, 1-thioxo-1,4-dihydro-2H-isoquinoline-3-ones and 1,4-dihydro-3(2H)-isoquinolones as CDK inhibitors and their preparation, pharmaceutical composition and use in the treatment of cancer, infections and other diseases
IN Tsou, Hwei-Ru; Ayral-Kaloustian, Semiramis; Birnberg, Gary Harold; Floyd, Middleton Brawner; Kaplan, Joshua; Kutterer, Kristina M. K.; Liu, Xiaoxiang; Nilakantan, Ramaswamy; Otteng, Mercy Adufa; Tang, Zhilian; Zask, Arie; Reich, Marvin; Tran, Tritan
PA Wyeth, John, and Brother Ltd., USA
SO PCT Int. Appl., 933pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007075783	A2	20070705	WO 2006-US48603	20061220
WO 2007075783	A3	20071122		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
US 20080085890	A1	20080410	US 2007-728897	20070326
PRAI US 2005-753701P	P	20051222		
WO 2006-US48603	A2	20061220		

OS MARPAT 147:166204

L5 ANSWER 4 OF 41 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2007:619346 CAPLUS
DN 147:52936
TI Preparation of alicyclic heterocycles as CCR4 function regulators
IN Furukubo, Shigeru; Miyazaki, Hiroshi
PA Tanabe Seiyaku Co., Ltd., Japan
SO PCT Int. Appl., 184pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007063934	A1	20070607	WO 2006-JP323908	20061130

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI JP 2005-348597 A 20051202
US 2005-750038P P 20051214
OS MARPAT 147:52936
RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 41 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2007:485607 CAPLUS
DN 146:482079
TI Preparation of 2-aminodihydrothiazine derivatives as β-secretase inhibitors
IN Kobayashi, Naotake; Ueda, Kazuo; Itoh, Naohiro; Suzuki, Shinji; Sakaguchi, Gaku; Kato, Akira; Yukimasa, Akira; Hori, Akihiro; Koriyama, Yuji; Haraguchi, Hidekazu; Yasui, Ken; Kanda, Yasuhiko
PA Japan
SO PCT Int. Appl., 330pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007049532	A1	20070503	WO 2006-JP321015	20061023

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,

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             KG, KZ, MD, RU, TJ, TM
PRAI JP 2005-309642       A     20051025
     JP 2006-76636        A     20060320
OS   MARPAT 146:482079
RE.CNT  45    THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT


=> d 6-10

L5   ANSWER 6 OF 41  CAPLUS  COPYRIGHT 2008 ACS on STN
AN   2007:409645  CAPLUS
DN   146:402010
TI   Preparation of substituted piperidinylpiperazine compounds with CXCR3
     antagonist activity
IN   Kim, Seong Heon; Shankar, Bandarpalle B.; Kozlowski, Joseph A.; Rosenblum,
     Stuart B.; Shih, Neng-Yang
PA   Schering Corp., USA
SO   U.S. Pat. Appl. Publ., 45pp.
     CODEN: USXXCO
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     ---------------     ----   --------    --------------------   --------
PI   US 20070082913       A1    20070412    US 2006-545201         20061010
     WO 2007047202        A1    20070426    WO 2006-US39404        20061010
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP,
             KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN,
             MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS,
             RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
             CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
             GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM
PRAI US 2005-725483P      P     20051011
OS   MARPAT 146:402010

L5   ANSWER 7 OF 41  CAPLUS  COPYRIGHT 2008 ACS on STN
AN   2007:143519  CAPLUS
DN   146:229382
TI   Preparation of dipiperazinyl ketones and related analogues as modulators
     of histamine H3 receptor binding
IN   Xie, Linghong; Ochterski, Joseph W.; Gao, Yang; Han, Bingsong; Caldwell,
     Timothy M.; Xu, Yuelian; Peterson, John M.; Ge, Ping; Ohliger, Robert
PA   Neurogen Corporation, USA
SO   PCT Int. Appl., 279pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     ---------------     ----   --------    --------------------   --------
PI   WO 2007016496        A2    20070208    WO 2006-US29761        20060728
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP,
             KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN,
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MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

AU 2006275568	A1	20070208	AU 2006-275568	20060728
CA 2606004	A1	20070208	CA 2006-2606004	20060728
US 20070049571	A1	20070301	US 2006-495986	20060728
EP 1909797	A2	20080416	EP 2006-788999	20060728

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, RS

PRAI US 2005-704722P	P	20050802	
WO 2006-US29761	W	20060728	

OS MARPAT 146:229382

L5 ANSWER 8 OF 41 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2006:886342 CAPLUS
DN 145:293103
TI Preparation of herteroaryl substituted pyrazinyl-piperazine-piperidines with CXCR3 antagonist activity
IN Zeng, Qingbei; Yang, De-Yi; Rosenblum, Stuart B.; Wong, Michael K. C.; Anilkumar, Gopinadhan N.; Kim, Seong Heon; Yu, Wensheng; Kozlowski, Joseph A.; Shih, Neng-Yang; Mcguinness, Brian F.; Zawacki, Lisa Guise; Hobbs, Douglas W.
PA Schering Corporation, USA; Pharmacopeia Drug Discovery, Inc.
SO PCT Int. Appl., 187pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006091428	A2	20060831	WO 2006-US5122	20060214
WO 2006091428	A3	20061102		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

AU 2006216941	A1	20060831	AU 2006-216941	20060214
CA 2598418	A1	20060831	CA 2006-2598418	20060214
US 20060276448	A1	20061207	US 2006-353474	20060214
EP 1858888	A2	20071128	EP 2006-758146	20060214

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU

KR 2007107040	A	20071106	KR 2007-718606	20070814
MX 200709949	A	20070926	MX 2007-9949	20070815
PRAI US 2005-653477P	P	20050216		
WO 2006-US5122	W	20060214		

OS MARPAT 145:293103

L5 ANSWER 9 OF 41 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2006:845712 CAPLUS
DN 145:271815
TI Heterocyclic-substituted piperazine-piperidines with CXCR3 antagonist activity and their preparation, pharmaceutical compositions, and use for treatment of chemokine-mediated diseases
IN Kim, Seong Heon; Anilkumar, Gopinadhan N.; Wong, Michael K. C.; Zeng, Qingbei; Rosenblum, Stuart B.; Kozlowski, Joseph A.; Shao, Yuefei; Mc Guinness, Brian F.; Hobbs, Douglas W.
PA Schering Corporation, USA; Pharmacopeia Drug Discovery, Inc.
SO PCT Int. Appl., 171pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2006088837	A2	20060824	WO 2006-US5123	20060214
	WO 2006088837	A3	20061102		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	AU 2006214477	A1	20060824	AU 2006-214477	20060214
	CA 2598456	A1	20060824	CA 2006-2598456	20060214
	US 20060276479	A1	20061207	US 2006-353641	20060214
	EP 1848710	A2	20071031	EP 2006-735000	20060214
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
	MX 200709945	A	20070926	MX 2007-9945	20070815
	IN 2007CN03575	A	20071116	IN 2007-CN3575	20070816
	KR 2007107046	A	20071106	KR 2007-718805	20070817
	NO 2007004690	A	20071116	NO 2007-4690	20070914
	CN 101163692	A	20080416	CN 2006-80012438	20071015
PRAI	US 2005-653309P	P	20050216		
	WO 2006-US5123	W	20060214		

OS MARPAT 145:271815

L5 ANSWER 10 OF 41 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2006:841716 CAPLUS
DN 145:271804
TI Pyrazinyl-substituted piperazine-piperidines with CXCR3 antagonist activity and their preparation, pharmaceutical composition, and their use for treatment of chemokine mediated diseases
IN Rosenblum, Stuart B.; Kim, Seong Heon; Zeng, Qingbei; Wong, Michael K. C.; Anilkumar, Gopinadhan N.; Jiang, Yueheng; Yu, Wensheng; Kozlowski, Joseph A.; Shih, Neng-Yang; Shankar, Bandarpalle B.; McGuinness, Brian F.; Dong, Guizhen; Zawacki, Lisa Guise; Hobbs, Douglas W.; Baldwin, John J.; Shao, Yuefei
PA Schering Corporation, USA; Pharmacopeia Drug Discovery, Inc.
SO PCT Int. Appl., 244 pp.
CODEN: PIXXD2

DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2006088921	A2	20060824	WO 2006-US5267	20060214
	WO 2006088921	A3	20061102		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	AU 2006214380	A1	20060824	AU 2006-214380	20060214
	CA 2598458	A1	20060824	CA 2006-2598458	20060214
	US 20070054919	A1	20070308	US 2006-354138	20060214
	EP 1856098	A2	20071121	EP 2006-735090	20060214
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
	MX 200709947	A	20070926	MX 2007-9947	20070815
	IN 2007CN03578	A	20071116	IN 2007-CN3578	20070816
	KR 2007107060	A	20071106	KR 2007-719297	20070823
	CN 101142209	A	20080312	CN 2006-80008141	20070913
	NO 2007004698	A	20071116	NO 2007-4698	20070914
PRAI	US 2005-653338P	P	20050216		
	WO 2006-US5267	W	20060214		

OS MARPAT 145:271804

=> d 11-15

L5 ANSWER 11 OF 41 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2006:410057 CAPLUS
DN 144:450732
TI Preparation of aromatic amides as inhibitors of c-fms kinase
IN Illig, Carl R.; Ballentine, Shelley K.; Chen, Jinsheng; Meegalla, Sanath; Rudolph, Jonathan; Wall, Mark J.; Wilson, Kenneth J.; Desjarlais, Renee; Manthey, Carl L.; Flores, Christopher M.; Molloy, Christopher J.
PA Janssen Pharmaceutica, N.V., Belg.
SO PCT Int. Appl., 170 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2006047504	A1	20060504	WO 2005-US38341	20051020
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,				

IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

	AU 2005299501	A1	20060504	AU 2005-299501	20051020
	US 20060100201	A1	20060511	US 2005-255043	20051020
	EP 1807407	A1	20070718	EP 2005-814104	20051020
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				
	CN 101084208	A	20071205	CN 2005-80043703	20051020
	IN 2007KN01562	A	20070727	IN 2007-KN1562	20070503
PRAI	US 2004-621192P	P	20041022		
	WO 2005-US38341	W	20051020		

OS MARPAT 144:450732
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 12 OF 41 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2005:1028086 CAPLUS
DN 143:326396
TI Preparation of piperidinyl- and piperazinyl-sulfonylmethyl hydroxamic acids and their use as protease inhibitors
IN Mcdonald, Joseph J.; Kassab, Darren J.; Massa, Mark A.; Grapperhaus, Margaret L.; Schmidt, Michelle A.; Rico, Joseph G.; Mullins, Patrick B.; Brown, David L.
PA USA
SO U.S. Pat. Appl. Publ., 417 pp., Cont.-in-part of U.S. Ser. No. 618,288.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 20050209278	A1	20050922	US 2003-700202	20031103
	US 20050009838	A1	20050113	US 2003-618288	20030425
	US 7119203	B2	20061010		
	CA 2543715	A1	20050512	CA 2004-2543715	20041103
	WO 2005042521	A2	20050512	WO 2004-US36666	20041103
	WO 2005042521	A3	20050707		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP 1689743	A2	20060816	EP 2004-810297	20041103
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				
	BR 2004015885	A	20070102	BR 2004-15885	20041103
	JP 2007510732	T	20070426	JP 2006-539634	20041103
	MX 2006PA04944	A	20060804	MX 2006-PA4944	20060503
PRAI	US 2002-375598P	P	20020425		
	US 2002-380713P	P	20020515		
	US 2002-392021P	P	20020627		
	US 2003-618288	A2	20030425		
	US 2003-700202	A	20031103		
	WO 2004-US36666	W	20041103		

OS CASREACT 143:326396; MARPAT 143:326396

L5 ANSWER 13 OF 41 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2005:409509 CAPLUS
DN 142:463765
TI Preparation of piperidinyl- and piperazinylsulfonylmethyl hydroxamic acids and their use as protease inhibitors
IN Brown, David L.; Grapperhaus, Margaret L.; Kassab, Darren J.; Massa, Mark A.; Mcdonald, Joseph J.; Mullins, Patrick B.; Rico, Joseph G.; Schmidt, Michelle A.
PA Pharmacia Corporation, USA
SO PCT Int. Appl., 644 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005042521	A2	20050512	WO 2004-US36666	20041103
	WO 2005042521	A3	20050707		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 20050209278	A1	20050922	US 2003-700202	20031103
	CA 2543715	A1	20050512	CA 2004-2543715	20041103
	EP 1689743	A2	20060816	EP 2004-810297	20041103
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				
	BR 2004015885	A	20070102	BR 2004-15885	20041103
	JP 2007510732	T	20070426	JP 2006-539634	20041103
	MX 2006PA04944	A	20060804	MX 2006-PA4944	20060503
PRAI	US 2003-700202	A	20031103		
	US 2002-375598P	P	20020425		
	US 2002-380713P	P	20020515		
	US 2002-392021P	P	20020627		
	US 2003-618288	A2	20030425		
	WO 2004-US36666	W	20041103		

OS CASREACT 142:463765; MARPAT 142:463765

L5 ANSWER 14 OF 41 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2005:141044 CAPLUS
DN 142:240465
TI Preparation of alkoxybenzoylpiperazines as inhibitors of glycine transporter 1 (GlyT-1)
IN Jolidon, Synese; Narquizian, Robert; Nettekoven, Matthias Heinrich; Norcross, Roger David; Pinard, Emmanuel; Stalder, Henri
PA F. Hoffmann-La Roche A.-G., Switz.
SO PCT Int. Appl., 241 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI WO 2005014563 A1 20050217 WO 2004-EP8633 20040802
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
AU 2004263306 A2 20050217 AU 2004-263306 20040802
AU 2004263306 A1 20050217
CA 2534675 A1 20050217 CA 2004-2534675 20040802
EP 1656361 A1 20060517 EP 2004-763703 20040802
EP 1656361 B1 20080102
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR
BR 2004013497 A 20061017 BR 2004-13497 20040802
CN 1867554 A 20061122 CN 2004-80029755 20040802
JP 2007501820 T 20070201 JP 2006-522944 20040802
AT 382611 T 20080115 AT 2004-763703 20040802
ES 2297458 T3 20080501 ES 2004-763703 20040802
US 20050209241 A1 20050922 US 2004-911359 20040804
US 7319099 B2 20080115
TW 289556 B 20071111 TW 2004-93123828 20040809
NO 2006000541 A 20060308 NO 2006-541 20060202
KR 774622 B1 20071108 KR 2006-702786 20060209
MX 2006PA01665 A 20060428 MX 2006-PA1665 20060210
IN 2006CN00506 A 20070706 IN 2006-CN506 20060210
PRAI EP 2003-17614 A 20030811
WO 2004-EP8633 W 20040802
OS MARPAT 142:240465
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 15 OF 41 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2005:120716 CAPLUS
DN 142:219312
TI Preparation of piperazine derivatives as stearoyl-CoA desaturase inhibitors for the treatment of diabetes and other diseases
IN Sviridov, Serguei; Kodumuru, Vishnumurthy; Liu, Shifeng; Abreo, Melwyn; Winther, Michael D.; Gschwend, Heinz W.; Kamboj, Rajender; Sun, Shaoyi; Holladay, Mark W.; Li, Wenbao; Tu, Chi
PA Xenon Pharmaceuticals Inc., Can.
SO PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 6

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005011657	A2	20050210	WO 2004-US24658	20040729
WO 2005011657	A3	20050324		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,

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             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
             EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
             SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
             SN, TD, TG
     AU 2004261268         A1    20050210    AU 2004-261268         20040729
     CA 2533901            A1    20050210    CA 2004-2533901        20040729
     EP 1651620            A2    20060503    EP 2004-779656         20040729
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR
     BR 2004012348         A     20060905    BR 2004-12348          20040729
     CN 1829701            A     20060906    CN 2004-80021942       20040729
     JP 2007500720         T     20070118    JP 2006-522096         20040729
     US 20060009459        A1    20060112    US 2005-55034          20050209
     MX 2006PA01206        A     20060920    MX 2006-PA1206         20060130
     US 20060252767        A1    20061109    US 2006-567009         20060130
     NO 2006000971         A     20060502    NO 2006-971            20060228
PRAI US 2003-491095P       P     20030730
     US 2004-546786P       P     20040223
     US 2004-546815P       P     20040223
     US 2004-546820P       P     20040223
     US 2004-546898P       P     20040223
     US 2004-546934P       P     20040223
     US 2004-553403P       P     20040316
     US 2004-553404P       P     20040316
     US 2004-553416P       P     20040316
     US 2004-553446P       P     20040316
     US 2004-553491P       P     20040316
     US 2004-901563        A2    20040729
     WO 2004-US24658       W     20040729
OS   CASREACT 142:219312; MARPAT 142:219312


=> d 16-20

L5   ANSWER 16 OF 41  CAPLUS  COPYRIGHT 2008 ACS on STN
AN   2003:892611  CAPLUS
DN   139:381375
TI   Preparation of amides as inhibitors of histone deacetylase
IN   Stokes, Elaine Sophie Elizabeth; Waring, Michael James; Gibson, Keith
     Hopkinson
PA   Astrazeneca AB, Swed.; Astrazeneca UK Limited
SO   PCT Int. Appl., 88 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
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PI   WO 2003092686        A1    20031113    WO 2003-GB1703         20030417
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
             PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT,
             TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     CA 2484065            A1    20031113    CA 2003-2484065        20030417
     AU 2003226553         A1    20031117    AU 2003-226553         20030417
     EP 1501508            A1    20050202    EP 2003-747499         20030417
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     EP 1501508           B1    20070221
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
     BR 2003009553        A     20050209    BR 2003-9553           20030417
     CN 1662236           A     20050831    CN 2003-814828         20030417
     JP 2005530748        T     20051013    JP 2004-500870         20030417
     AT 354366            T     20070315    AT 2003-747499         20030417
     ES 2280768           T3    20070916    ES 2003-747499         20030417
     IN 2004DN03153       A     20050401    IN 2004-DN3153         20041013
     NO 2004004557        A     20041022    NO 2004-4557           20041022
     US 20050222410       A1    20051006    US 2004-512808         20041026
     MX 2004PA10686       A     20041213    MX 2004-PA10686        20041027
     HK 1072365           A1    20070706    HK 2005-105019         20050615
PRAI GB 2002-9715         A     20020427
     WO 2003-GB1703       W     20030417
OS   MARPAT 139:381375
RE.CNT  4     THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5   ANSWER 17 OF 41  CAPLUS  COPYRIGHT 2008 ACS on STN
AN   2003:875282  CAPLUS
DN   139:364961
TI   Preparation of piperidinyl-and piperazinyl-sulfonylmethyl hydroxamic acids
     and their use as protease inhibitors
IN   Barta, Thomas E.; Becker, Daniel P.; Bedell, Louis J.; Boehm, Terri L.;
     Brown, David L.; Carroll, Jeffery N.; Chen, Yiyuan; Fobian, Yvette;
     Freskos, John N.; Gasiecki, Alan F.; Grapperhaus, Margaret; Heintz, Robert
     M.; Hockerman, Susan L.; Kassab, Darren J.; Khanna, Ish Kumar; Kolodziej,
     Stephen A.; Massa, Mark; Mcdonald, Joseph; Mischke, Brent V.; Mischke,
     Deborah A.; Mullins, Patrick B.; Nagy, Mark; Norton, Monica B.; Rico,
     Joseph G.; Schmidt, Michelle A.; Stehle, Nathan W.; Talley, John J.;
     Vernier, William F.; Villamill, Clara I.; Wang, Lijuan Jane; Wynn, Thomas
     A.
PA   Pharmacia Corporation, USA; et al.
SO   PCT Int. Appl., 819 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 3
     PATENT NO.           KIND   DATE        APPLICATION NO.        DATE
     ---------------      ----   --------    -------------------    --------
PI   WO 2003091247         A2    20031106    WO 2003-US13123        20030425
     WO 2003091247         A3    20040115
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
             PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT,
             TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     CA 2483314            A1    20031106    CA 2003-2483314        20030425
     AU 2003221786         A1    20031110    AU 2003-221786         20030425
     EP 1501827            A2    20050202    EP 2003-718529         20030425
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
     BR 2003009671         A     20050503    BR 2003-9671           20030425
     JP 2005537228         T     20051208    JP 2003-587805         20030425
     MX 2004PA10555        A     20050217    MX 2004-PA10555        20041022
PRAI US 2002-375598P       P     20020425
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     US 2002-380713P      P     20020515
     US 2002-392021P      P     20020627
     WO 2003-US13123      W     20030425
OS   MARPAT 139:364961

L5   ANSWER 18 OF 41  CAPLUS  COPYRIGHT 2008 ACS on STN
AN   2003:737742  CAPLUS
DN   139:276884
TI   Preparation of sulfonyl-derivatives as novel inhibitors of histone
     deacetylase
IN   Van Emelen, Kristof; Arts, Janine; Backx, Leo Jacobus Jozef; De Winter,
     Hans Louis Jos; Van Brandt, Sven Franciscus Anna; Verdonck, Marc Gustaaf
     Celine; Meerpoel, Lieven; Pilatte, Isabelle Noeelle Constance; Poncelet,
     Virginie Sophie; Dyatkin, Alexey Borisovich
PA   Janssen Pharmaceutica N.V., Belg.; et al.
SO   PCT Int. Appl., 139 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 8
     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
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PI   WO 2003076422         A1    20030918    WO 2003-EP2516          20030311
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     CA 2476586            A1    20030918    CA 2003-2476586         20030311
     AU 2003218738         A1    20030922    AU 2003-218738          20030311
     EP 1485365            A1    20041215    EP 2003-711982          20030311
     EP 1485365            B1    20080514
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
     BR 2003007575         A     20041221    BR 2003-7575            20030311
     CN 1642931            A     20050720    CN 2003-805952          20030311
     JP 2005525380         T     20050825    JP 2003-574641          20030311
     NZ 534830             A     20050826    NZ 2003-534830          20030311
     CN 101007803          A     20070801    CN 2007-10005212        20030311
     MX 2004PA07775        A     20041015    MX 2004-PA7775          20040811
     IN 2004DN02524        A     20070413    IN 2004-DN2524          20040830
     US 20050113373        A1    20050526    US 2004-507708          20040913
     US 7205304            B2    20070417
     NO 2004004314         A     20041012    NO 2004-4314            20041012
     US 20070142393        A1    20070621    US 2007-668906          20070130
     US 20080108601        A1    20080508    US 2007-926759          20071029
PRAI US 2002-363799P       P     20020313
     US 2002-420989P       P     20021024
     WO 2002-EP14833       A     20021223
     CN 2003-805921        A3    20030311
     WO 2003-EP2516        W     20030311
     US 2004-507708        A3    20040913
     US 2007-668906        A1    20070130
OS   MARPAT 139:276884
RE.CNT  2     THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT
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L5 ANSWER 19 OF 41 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2003:472489 CAPLUS
DN 139:53037
TI Preparation of substituted heterocyclic carboxamides with antithrombotic activity
IN Herron, David Kent; Joseph, Sajan; Marquart, Angela Lynn; Masters, John Joseph; Mendel, David; Smith, Gerald Floyd; Tebbe, Anne Louise; Waid, Philip Parker; Wiley, Michael Robert; Yee, Ying Kwong
PA Eli Lilly and Company, USA; et al.
SO PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003050088	A1	20030619	WO 2002-US36139	20021202
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002350172	A1	20030623	AU 2002-350172	20021202
EP 1456175	A1	20040915	EP 2002-786700	20021202
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
US 20040242581	A1	20041202	US 2004-497250	20040528
PRAI US 2001-338337P	P	20011207		
WO 2002-US36139	W	20021202		

OS MARPAT 139:53037
RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 20 OF 41 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2003:356416 CAPLUS
DN 138:368914
TI Preparation of indole- and pyrrolo[2,3-b]pyridine-containing amide derivatives as antagonists of transforming growth factor-β (TGF-β)
IN Maruyama, Yasufumi; Hirabayashi, Kazuko; Hori, Katsutoshi
PA Nippon Shinyaku Co., Ltd., Japan
SO PCT Int. Appl., 123 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003037862	A1	20030508	WO 2002-JP11232	20021029
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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     AU 2002344424         A1    20030512    AU 2002-344424         20021029
     EP 1452525            A1    20040901    EP 2002-779936         20021029
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
     US 20050014942        A1    20050120    US 2004-494622         20040430
PRAI JP 2001-332942        A     20011030
     JP 2002-127771        A     20020430
     WO 2002-JP11232       W     20021029
OS   MARPAT 138:368914
RE.CNT  22    THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT


=> d 16-20 ibib abs hitstr

L5   ANSWER 16 OF 41  CAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:        2003:892611  CAPLUS
DOCUMENT NUMBER:         139:381375
TITLE:                   Preparation of amides as inhibitors of histone
                         deacetylase
INVENTOR(S):             Stokes, Elaine Sophie Elizabeth; Waring, Michael
                         James; Gibson, Keith Hopkinson
PATENT ASSIGNEE(S):      Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE:                  PCT Int. Appl., 88 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
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     WO 2003092686         A1    20031113    WO 2003-GB1703          20030417
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
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             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
             PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT,
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     CA 2484065            A1    20031113    CA 2003-2484065         20030417
     AU 2003226553         A1    20031117    AU 2003-226553          20030417
     EP 1501508            A1    20050202    EP 2003-747499          20030417
     EP 1501508            B1    20070221
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     BR 2003009553         A     20050209    BR 2003-9553            20030417
     CN 1662236            A     20050831    CN 2003-814828          20030417
     JP 2005530748         T     20051013    JP 2004-500870          20030417
     AT 354366             T     20070315    AT 2003-747499          20030417
     ES 2280768            T3    20070916    ES 2003-747499          20030417
     IN 2004DN03153        A     20050401    IN 2004-DN3153          20041013
     NO 2004004557         A     20041022    NO 2004-4557            20041022
     US 20050222410        A1    20051006    US 2004-512808          20041026
     MX 2004PA10686        A     20041213    MX 2004-PA10686         20041027
     HK 1072365            A1    20070706    HK 2005-105019          20050615
PRIORITY APPLN. INFO.:                       GB 2002-9715         A  20020427
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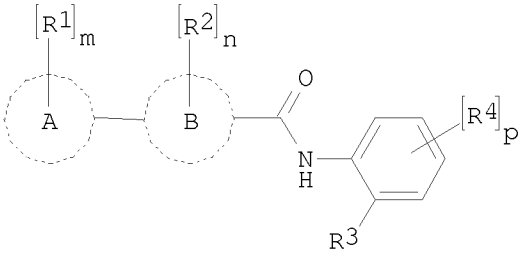
WO 2003-GB1703 W 20030417

OTHER SOURCE(S): MARPAT 139:381375

GI



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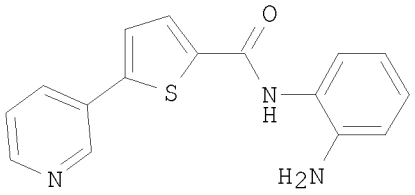


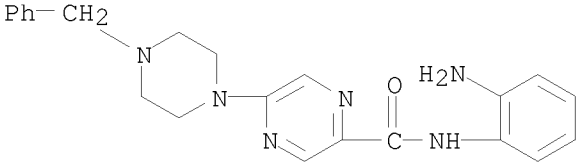
II

AB The title compds. [I; ring A = heterocyclyl; m = 0-4; R1 = OH, halo, CF3, CN; ring B = thienyl, thiadiazolyl, thiazolyl, pyrimidyl, pyrazinyl, pyridazinyl and pyridyl; R2 = halo; n = 0-2; R4 = OH, halo, CF3, CN; p = 0-4; R3 = NH2, OH] or pharmaceutically acceptable salts or in-vivo hydrolysable ester or amide thereof, useful in the treatment of diseases or medical conditions mediated by histone deacetylase such as cancer, were prepared Thus, coupling N-(2-tert-butoxycarbonylaminophenyl)-5-bromothiophene-2-carboxamide with pyridine-3-boronic acid in the presence of Pd(PPh3)4 followed by Boc-group removal afforded II. The compds. I showed IC50 of < 2.5 μM against recombinant human HDAC1 produced in Hi5 insect cells. The pharmaceutical compns. containing the compound I are claimed.

IT 623587-27-9P 623587-30-4P 623587-31-5P
623587-32-6P 623587-33-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amides as inhibitors of histone deacetylase)

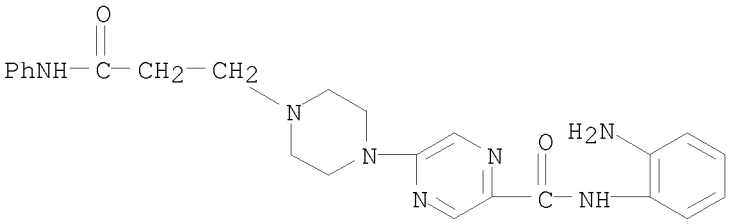
RN 623587-27-9 CAPLUS

CN 2-Pyrazinecarboxamide, N-(2-aminophenyl)-5-[4-(phenylmethyl)-1-piperazinyl]- (CA INDEX NAME)



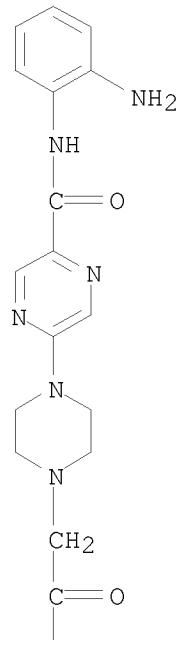
RN 623587-30-4 CAPLUS

CN 2-Pyrazinecarboxamide, N-(2-aminophenyl)-5-[4-[3-oxo-3-(phenylamino)propyl]-1-piperazinyl]- (CA INDEX NAME)

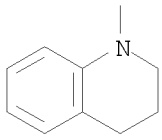


RN 623587-31-5 CAPLUS
CN 2-Pyrazinecarboxamide, N-(2-aminophenyl)-5-[4-[2-(3,4-dihydro-1(2H)-quinolinyl)-2-oxoethyl]-1-piperazinyl]- (CA INDEX NAME)

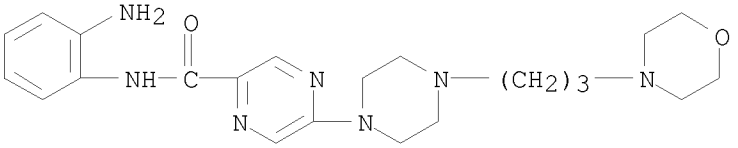
PAGE 1-A



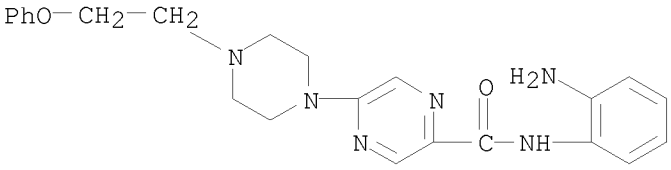
PAGE 2-A



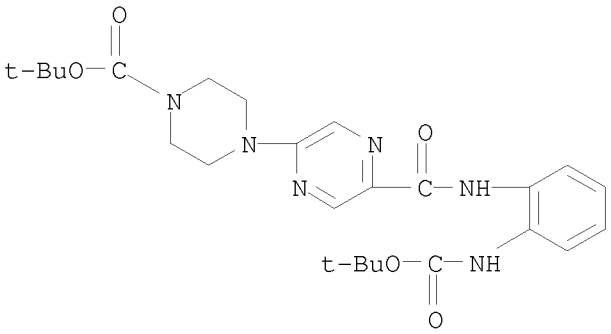
RN 623587-32-6 CAPLUS
CN 2-Pyrazinecarboxamide, N-(2-aminophenyl)-5-[4-[3-(4-morpholinyl)propyl]-1-piperazinyl]- (CA INDEX NAME)



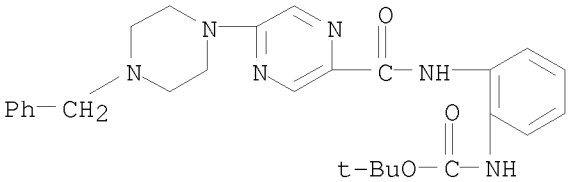
RN 623587-33-7 CAPLUS
CN 2-Pyrazinecarboxamide, N-(2-aminophenyl)-5-[4-(2-phenoxyethyl)-1-piperazinyl]- (CA INDEX NAME)



IT 623588-15-8P 623588-16-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of amides as inhibitors of histone deacetylase)
RN 623588-15-8 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[5-[[[2-[[(1,1-dimethylethoxy)carbonyl]amino]phenyl]amino]carbonyl]-2-pyrazinyl]-, 1,1-dimethylethyl ester (CA INDEX NAME)



RN 623588-16-9 CAPLUS
CN Carbamic acid, [2-[[[5-[4-(phenylmethyl)-1-piperazinyl]pyrazinyl]carbonyl]amino]phenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 17 OF 41 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:875282 CAPLUS
DOCUMENT NUMBER: 139:364961
TITLE: Preparation of piperidinyl-and piperazinyl-sulfonylmethyl hydroxamic acids and their use as protease inhibitors
INVENTOR(S): Barta, Thomas E.; Becker, Daniel P.; Bedell, Louis J.; Boehm, Terri L.; Brown, David L.; Carroll, Jeffery N.; Chen, Yiyuan; Fobian, Yvette; Freskos, John N.; Gasiecki, Alan F.; Grapperhaus, Margaret; Heintz, Robert M.; Hockerman, Susan L.; Kassab, Darren J.; Khanna, Ish Kumar; Kolodziej, Stephen A.; Massa, Mark; Mcdonald, Joseph; Mischke, Brent V.; Mischke, Deborah A.; Mullins, Patrick B.; Nagy, Mark; Norton, Monica B.; Rico, Joseph G.; Schmidt, Michelle A.; Stehle, Nathan W.; Talley, John J.; Vernier, William F.; Villamill, Clara I.; Wang, Lijuan Jane; Wynn, Thomas A.
PATENT ASSIGNEE(S): Pharmacia Corporation, USA; et al.
SOURCE: PCT Int. Appl., 819 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003091247	A2	20031106	WO 2003-US13123	20030425
WO 2003091247	A3	20040115		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2483314	A1	20031106	CA 2003-2483314	20030425
AU 2003221786	A1	20031110	AU 2003-221786	20030425
EP 1501827	A2	20050202	EP 2003-718529	20030425
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003009671	A	20050503	BR 2003-9671	20030425
JP 2005537228	T	20051208	JP 2003-587805	20030425
MX 2004PA10555	A	20050217	MX 2004-PA10555	20041022

PRIORITY APPLN. INFO.:

US 2002-375598P	P	20020425
US 2002-380713P	P	20020515
US 2002-392021P	P	20020627
WO 2003-US13123	W	20030425

OTHER SOURCE(S): MARPAT 139:364961
GI

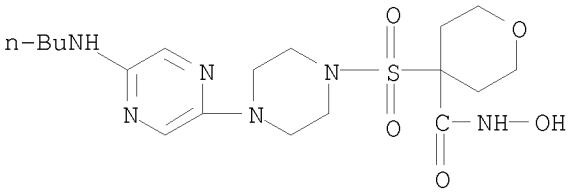
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [A1 and A2 together with the C to which they are bonded join to form (un)substituted-heterocyclyl or -carbocyclyl, or A1 and A2 are independently selected from H, alkyl, alkoxyalkyl, alkenyl, alkynyl,

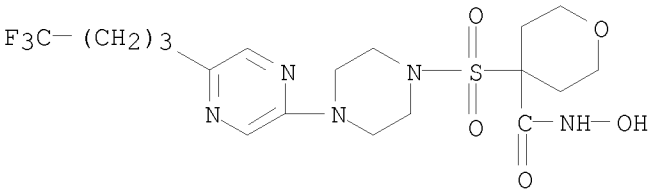
etc.; Rx = H, halo, CN, OH, NO2, alkyl, alkenyl, alkoxy, alkoxyalkyl, heterocyclyl, etc.; Y = N, CH, or CRx; E1 = (un)substituted heteroaryl; E2 = O, CO, C(O)O, OC(O), bond, S, etc.; E3 = halo, CN, (un)substituted-alkyl, -alkenyl, -alkynyl, -heterocyclyl, heterocyclylalkyl, etc.] and their pharmaceutically acceptable salts are prepared and disclosed as protease inhibitors. Thus, e.g., II·HCl was prepared with piperazine ring formation occurring via cyclization of 2,2,2-trifluoroethoxyaniline (preparation given) with N,N-di(2-chloroethyl)methylsulfonamide (preparation given) to provide piperazinyl intermediate III which was converted in five addnl. steps to the desired product. This invention is directed generally to proteinase (also known as 'protease') inhibitors, and more particularly, inhibitors of matrix metalloproteinase (also known as 'matrix metalloprotease' or 'MMP') activity and/or aggrecanase activity. In assays to determine inhibition consts. (Ki) against MMP-1, MMP-2, MMP-9, MMP-13 and MMP-14, I possessed values ranging from 0.13->10,000. This invention also is directed to compns. of such hydroxamic acids, intermediates for the syntheses of such hydroxamic acids, methods for making such hydroxamic acids, and methods for treating conditions (particularly pathol. conditions) associated with MMP activity and/or aggrecanase activity.

IT 622393-73-1P 622393-74-2P 622393-75-3P
622393-76-4P 622393-77-5P 622393-79-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(claimed compds.; preparation of piperidinyl-and piperazinyl-sulfonylmethyl hydroxamic acids and their use as matrix metalloproteinase inhibitors)

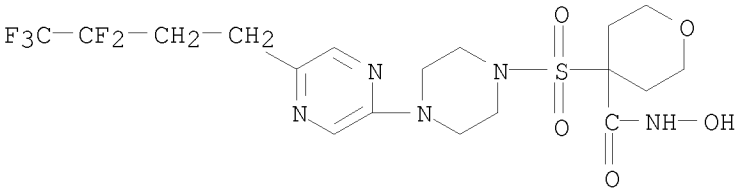
RN 622393-73-1 CAPLUS
CN 2H-Pyran-4-carboxamide, 4-[[4-[5-(butylamino)-2-pyrazinyl]-1-piperazinyl]sulfonyl]tetrahydro-N-hydroxy- (CA INDEX NAME)



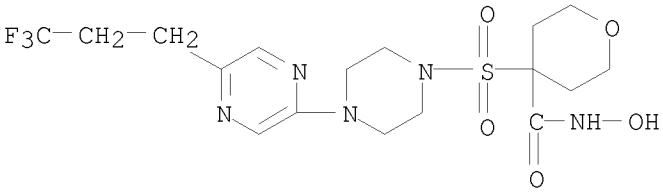
RN 622393-74-2 CAPLUS
CN 2H-Pyran-4-carboxamide, tetrahydro-N-hydroxy-4-[[4-[5-(4,4,4-trifluorobutyl)-2-pyrazinyl]-1-piperazinyl]sulfonyl]- (CA INDEX NAME)



RN 622393-75-3 CAPLUS
CN 2H-Pyran-4-carboxamide, tetrahydro-N-hydroxy-4-[[4-[5-(3,3,4,4,4-pentafluorobutyl)-2-pyrazinyl]-1-piperazinyl]sulfonyl]- (CA INDEX NAME)



RN 622393-76-4 CAPLUS
CN 2H-Pyran-4-carboxamide, tetrahydro-N-hydroxy-4-[[4-[5-(3,3,3-trifluoropropyl)-2-pyrazinyl]-1-piperazinyl]sulfonyl]- (CA INDEX NAME)



RN 622393-77-5 CAPLUS
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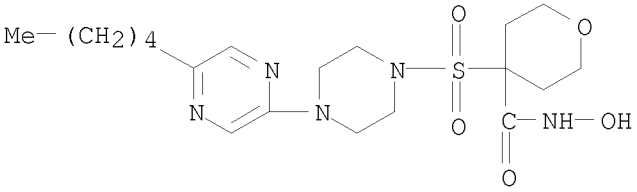
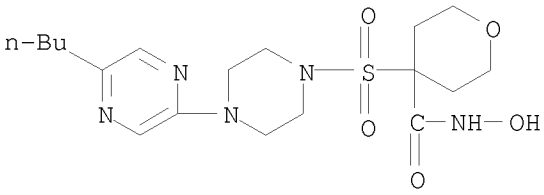


RN 622393-79-7 CAPLUS
CN 2H-Pyran-4-carboxamide, 4-[[4-(5-butyl-2-pyrazinyl)-1-piperazinyl]sulfonyl]tetrahydro-N-hydroxy- (CA INDEX NAME)



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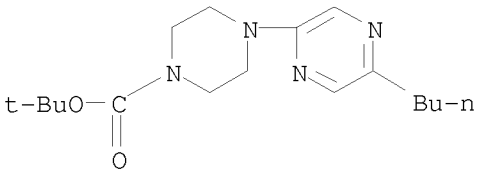
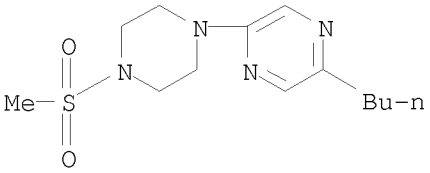
622386-12-3P 622386-13-4P 622386-14-5P
622390-14-1P 622390-15-2P 622390-16-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of piperidinyl-and piperazinyl-sulfonylmethyl hydroxamic acids and their use as matrix metalloproteinase inhibitors)

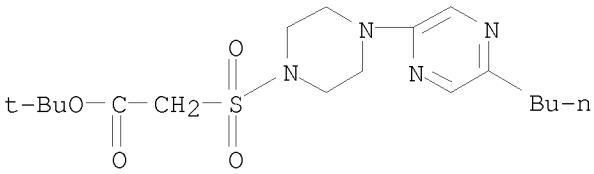
RN 622386-09-8 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-(5-butyl-2-pyrazinyl)-, 1,1-dimethylethyl ester (CA INDEX NAME)



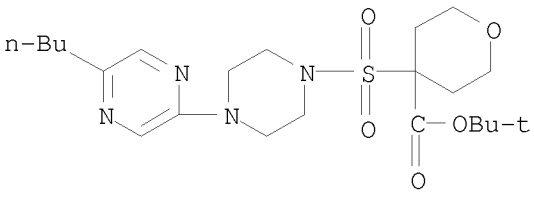
RN 622386-10-1 CAPLUS
CN Pyrazine, 2-butyl-5-[4-(methylsulfonyl)-1-piperazinyl]- (CA INDEX NAME)



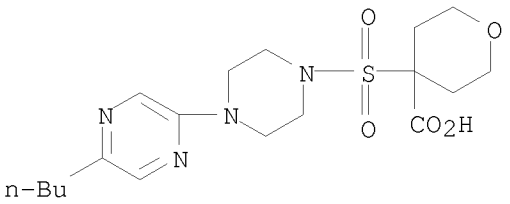
RN 622386-11-2 CAPLUS
CN Acetic acid, 2-[[4-(5-butyl-2-pyrazinyl)-1-piperazinyl]sulfonyl]-, 1,1-dimethylethyl ester (CA INDEX NAME)



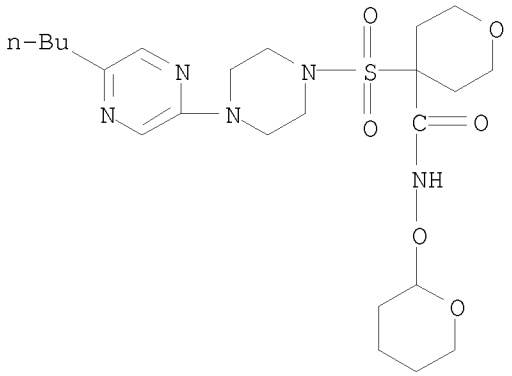
RN 622386-12-3 CAPLUS
CN 2H-Pyran-4-carboxylic acid, 4-[[4-(5-butyl-2-pyrazinyl)-1-piperazinyl]sulfonyl]tetrahydro-, 1,1-dimethylethyl ester (CA INDEX NAME)



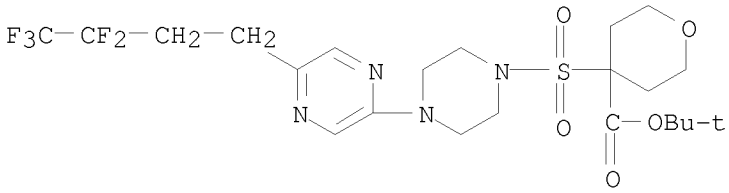
RN 622386-13-4 CAPLUS
CN 2H-Pyran-4-carboxylic acid, 4-[[4-(5-butyl-2-pyrazinyl)-1-piperazinyl]sulfonyl]tetrahydro- (CA INDEX NAME)



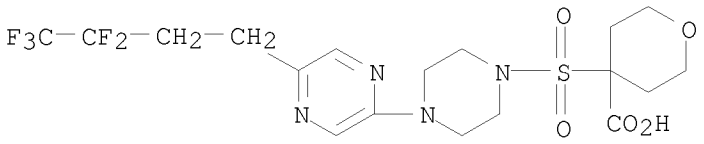
RN 622386-14-5 CAPLUS
CN 2H-Pyran-4-carboxamide, 4-[[4-(5-butyl-2-pyrazinyl)-1-piperazinyl]sulfonyl]tetrahydro-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (CA INDEX NAME)



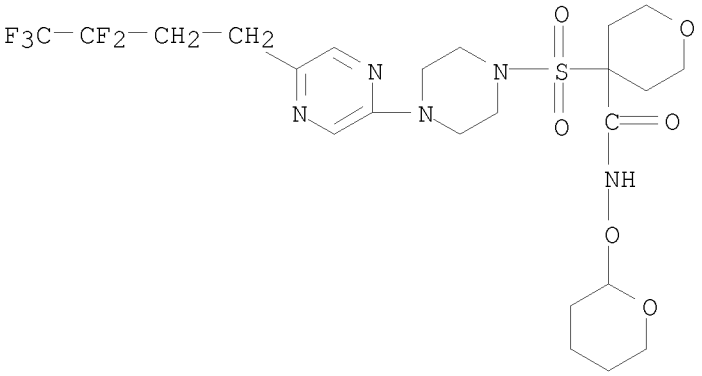
RN 622390-14-1 CAPLUS
CN 2H-Pyran-4-carboxylic acid, tetrahydro-4-[[4-[5-(3,3,4,4,4-pentafluorobutyl)-2-pyrazinyl]-1-piperazinyl]sulfonyl]-, 1,1-dimethylethyl ester (CA INDEX NAME)



RN 622390-15-2 CAPLUS
CN 2H-Pyran-4-carboxylic acid, tetrahydro-4-[[4-[5-(3,3,4,4,4-pentafluorobutyl)-2-pyrazinyl]-1-piperazinyl]sulfonyl]- (CA INDEX NAME)



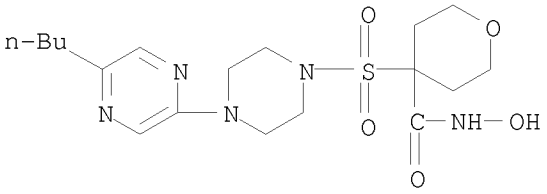
RN 622390-16-3 CAPLUS
CN 2H-Pyran-4-carboxamide, tetrahydro-4-[[4-[5-(3,3,4,4,4-pentafluorobutyl)-2-pyrazinyl]-1-piperazinyl]sulfonyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (CA INDEX NAME)



IT 622381-75-3P 622382-14-3P 622383-94-2P
622383-95-3P 622384-03-6P 622384-04-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperidinyl-and piperazinyl-sulfonylmethyl hydroxamic acids and their use as matrix metalloproteinase inhibitors)

RN 622381-75-3 CAPLUS

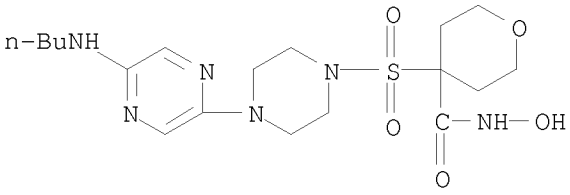
CN 2H-Pyran-4-carboxamide, 4-[[4-(5-butyl-2-pyrazinyl)-1-piperazinyl]sulfonyl]tetrahydro-N-hydroxy-, hydrochloride (1:2) (CA INDEX NAME)



●2 HCl

RN 622382-14-3 CAPLUS

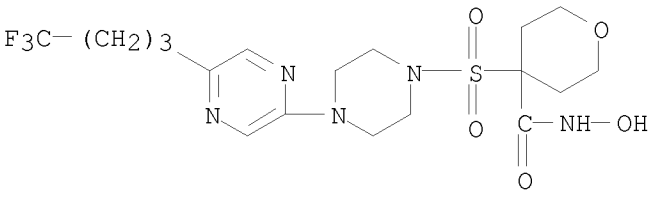
CN 2H-Pyran-4-carboxamide, 4-[[4-[5-(butylamino)-2-pyrazinyl]-1-piperazinyl]sulfonyl]tetrahydro-N-hydroxy-, hydrochloride (1:2) (CA INDEX NAME)



●2 HCl

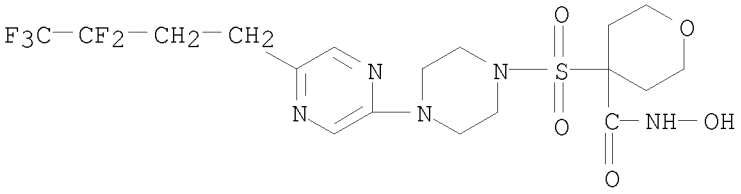
RN 622383-94-2 CAPLUS

CN 2H-Pyran-4-carboxamide, tetrahydro-N-hydroxy-4-[[4-[5-(4,4,4-trifluorobutyl)-2-pyrazinyl]-1-piperazinyl]sulfonyl]-, hydrochloride (1:2) (CA INDEX NAME)



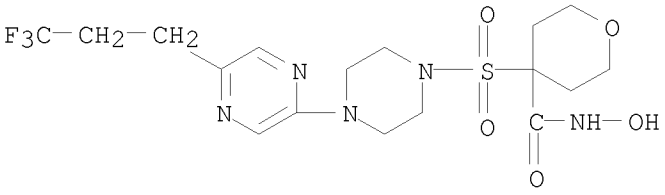
● 2 HCl

RN 622383-95-3 CAPLUS
CN 2H-Pyran-4-carboxamide, tetrahydro-N-hydroxy-4-[[4-[5-(3,3,4,4,4-pentafluorobutyl)-2-pyrazinyl]-1-piperazinyl]sulfonyl]-, hydrochloride (1:2) (CA INDEX NAME)



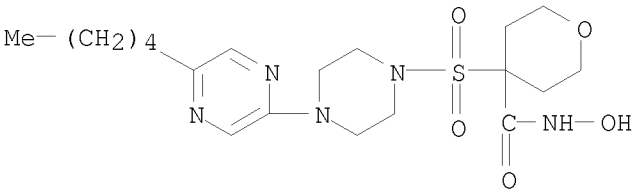
● 2 HCl

RN 622384-03-6 CAPLUS
CN 2H-Pyran-4-carboxamide, tetrahydro-N-hydroxy-4-[[4-[5-(3,3,3-trifluoropropyl)-2-pyrazinyl]-1-piperazinyl]sulfonyl]-, hydrochloride (1:2) (CA INDEX NAME)



● 2 HCl

RN 622384-04-7 CAPLUS
CN 2H-Pyran-4-carboxamide, tetrahydro-N-hydroxy-4-[[4-(5-pentyl-2-pyrazinyl)-1-piperazinyl]sulfonyl]-, hydrochloride (1:2) (CA INDEX NAME)



●2 HCl

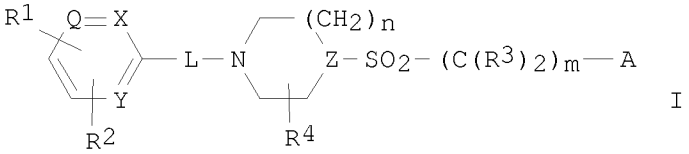
L5 ANSWER 18 OF 41 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:737742 CAPLUS
DOCUMENT NUMBER: 139:276884
TITLE: Preparation of sulfonyl-derivatives as novel inhibitors of histone deacetylase
INVENTOR(S): Van Emelen, Kristof; Arts, Janine; Backx, Leo Jacobus Jozef; De Winter, Hans Louis Jos; Van Brandt, Sven Franciscus Anna; Verdonck, Marc Gustaaf Celine; Meerpoel, Lieven; Pilatte, Isabelle Noeelle Constance; Poncelet, Virginie Sophie; Dyatkin, Alexey Borisovich
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.; et al.
SOURCE: PCT Int. Appl., 139 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003076422	A1	20030918	WO 2003-EP2516	20030311
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2476586	A1	20030918	CA 2003-2476586	20030311
AU 2003218738	A1	20030922	AU 2003-218738	20030311
EP 1485365	A1	20041215	EP 2003-711982	20030311
EP 1485365	B1	20080514		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003007575	A	20041221	BR 2003-7575	20030311
CN 1642931	A	20050720	CN 2003-805952	20030311
JP 2005525380	T	20050825	JP 2003-574641	20030311
NZ 534830	A	20050826	NZ 2003-534830	20030311
CN 101007803	A	20070801	CN 2007-10005212	20030311
MX 2004PA07775	A	20041015	MX 2004-PA7775	20040811
IN 2004DN02524	A	20070413	IN 2004-DN2524	20040830
US 20050113373	A1	20050526	US 2004-507708	20040913
US 7205304	B2	20070417		
NO 2004004314	A	20041012	NO 2004-4314	20041012

US 20070142393	A1	20070621	US 2007-668906		20070130
US 20080108601	A1	20080508	US 2007-926759		20071029
PRIORITY APPLN. INFO.:			US 2002-363799P	P	20020313
			US 2002-420989P	P	20021024
			WO 2002-EP14833	A	20021223
			CN 2003-805921	A3	20030311
			WO 2003-EP2516	W	20030311
			US 2004-507708	A3	20040913
			US 2007-668906	A1	20070130

OTHER SOURCE(S): MARPAT 139:276884

GI



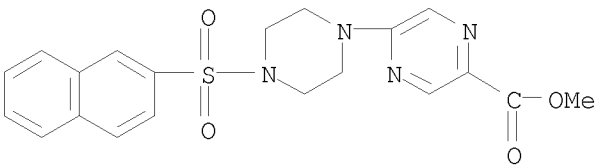
I

AB This invention comprises the novel compds. (I) (wherein n = 1-3, m = 1-4, Q, X, Y = N, CH; Z = N, CH; R1 = (un)substituted amido, acylamido, guandido, and other Zn chelating group, etc.; R2 = H, halo, OH, NH2, NO2, C1-6alkyl, C1-6alkoxy, CF3, di(C1-6alkyl)amino, HONH, naphthalenylsulfonylpyrazinyl; R3 = H aryl; R4 = H, HO, NH2, hydroxyC1-6alkyl, C1-6alkyl, C1-6alkoxy, arylC1-6alkyl, aminocarbonyl, hydroxycarbonyl, aminoC1-6alkyl, aminocarbonylC1-6alkyl, hydroxycarbonylC1-6alkyl, hydroxyaminocarbonyl, C1-6alkoxycarbonyl, C1-6alkylamino, di(C1-6alkyl)aminoC1-6alkyl; L = nul or bivalent radical selected from C1-6alkanediyl, amino, carbonyl or aminocarbonyl; A = aryl, cyclohexyl, heterocyclic derivs.), having histone deacetylase inhibiting enzymic activity; their preparation, compns. containing them and their use as a medicine. For example, 4-(4-(2-naphthylsulfonyl)piperazin-1-yl)-N-hydroxybenzamide in 100% yield was prepared by the hydrogenation of 4-(4-(2-naphthylsulfonyl)piperazin-1-yl)-N-(phenylmethoxy)benzamide (II) in THF by Pd/C as a catalyst. II was prepared from 1,1-dimethylethyl 4-(4-carboxyphenyl)-1-piperazinecarboxylate and O-(phenylmethyl)hydroxylamine hydrochloride in presence of dimethylaminopyridine in CH2Cl2 and diisopropylcarbodiimide, forming 1,1-dimethylethyl 4-[4-[(phenylmethoxy)amino]carbonylphenyl]-1-piperazinecarboxylate which was saponified and subsequently reacted with 2-naphthalenesulfonyl chloride to give the II.

IT 604768-44-7P 604768-45-8P 604768-46-9P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation of sulfonyl derivs. as histone deacetylase inhibitors and antitumor agent for treatment of cancer)

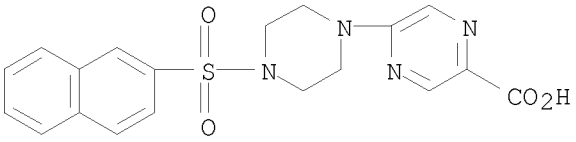
RN 604768-44-7 CAPLUS

CN 2-Pyrazinecarboxylic acid, 5-[4-(2-naphthalenylsulfonyl)-1-piperazinyl]-, methyl ester (CA INDEX NAME)

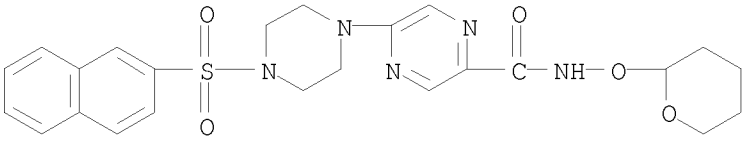


RN 604768-45-8 CAPLUS

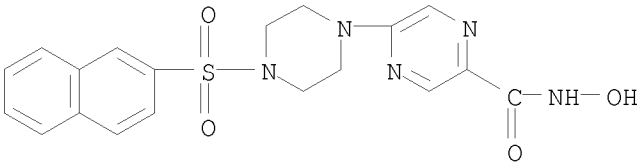
CN 2-Pyrazinecarboxylic acid, 5-[4-(2-naphthalenylsulfonyl)-1-piperazinyl]- (CA INDEX NAME)



RN 604768-46-9 CAPLUS
CN 2-Pyrazinecarboxamide, 5-[4-(2-naphthalenylsulfonyl)-1-piperazinyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (CA INDEX NAME)



IT 604769-14-4P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of sulfonyl derivs. as histone deacetylase inhibitors and antitumor agent for treatment of cancer)
RN 604769-14-4 CAPLUS
CN 2-Pyrazinecarboxamide, N-hydroxy-5-[4-(2-naphthalenylsulfonyl)-1-piperazinyl]- (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 19 OF 41 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:472489 CAPLUS
DOCUMENT NUMBER: 139:53037
TITLE: Preparation of substituted heterocyclic carboxamides with antithrombotic activity
INVENTOR(S): Herron, David Kent; Joseph, Sajan; Marquart, Angela Lynn; Masters, John Joseph; Mendel, David; Smith, Gerald Floyd; Tebbe, Anne Louise; Waid, Philip Parker; Wiley, Michael Robert; Yee, Ying Kwong
PATENT ASSIGNEE(S): Eli Lilly and Company, USA; et al.
SOURCE: PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

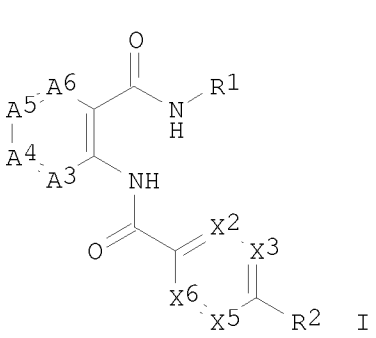
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2003050088	A1	20030619	WO 2002-US36139	20021202
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002350172	A1	20030623	AU 2002-350172	20021202
EP 1456175	A1	20040915	EP 2002-786700	20021202
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
US 20040242581	A1	20041202	US 2004-497250	20040528

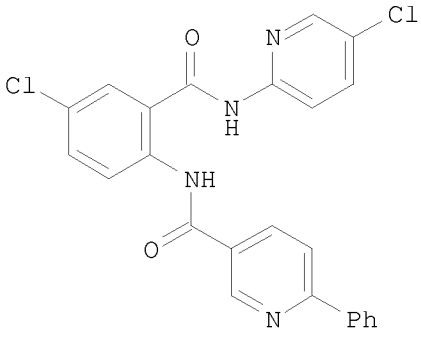
PRIORITY APPLN. INFO.: US 2001-338337P P 20011207
WO 2002-US36139 W 20021202

OTHER SOURCE(S): MARPAT 139:53037

GI



I



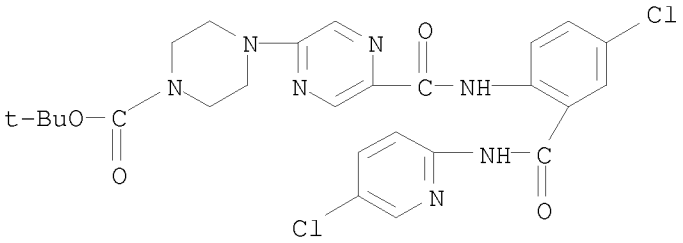
II

AB The title compds. [I; A3-A6, together with the two carbons to which they are attached, complete a substituted benzene or pyridine; R1 = (un)substituted 2-pyridyl; one or two of X1-X4 = N and each of others of X1-X4 = CH; R2 = (un)substituted Ph, 5-6 membered heteroaryl, etc.], useful as inhibitors of factor Xa, were prepared Thus, coupling 5-chloro-2-(6-chloropyridin-3-ylcarbonylamino)-N-(5-chloropyridin-2-yl)benzamide (preparation given) with phenylboronic acid afforded the pyridinecarboxamide II. In general, the compds. I exhibit a Kass of 3-10x106 L/Mol or greater against factor Xa (Kass is calculated for a range of concns. of test compds. which produce hydrolysis inhibition between 20% and 80% of control and the mean value reported in units of liter per mol).

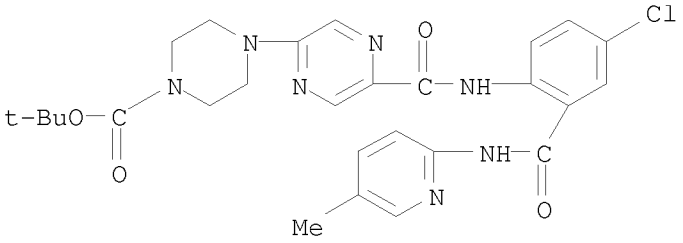
IT 545436-24-6P 545436-25-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of substituted heterocyclic carboxamides with antithrombotic activity)

RN 545436-24-6 CAPLUS

CN 1-Piperazinecarboxylic acid, 4-[5-[[[4-chloro-2-[[(5-chloro-2-pyridinyl)amino]carbonyl]phenyl]amino]carbonyl]-2-pyrazinyl]-, 1,1-dimethylethyl ester (CA INDEX NAME)



RN 545436-25-7 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[5-[[[4-chloro-2-[[(5-methyl-2-pyridinyl)amino]carbonyl]phenyl]amino]carbonyl]-2-pyrazinyl]-, 1,1-dimethylethyl ester (CA INDEX NAME)



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 20 OF 41 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:356416 CAPLUS
DOCUMENT NUMBER: 138:368914
TITLE: Preparation of indole- and pyrrolo[2,3-b]pyridine-containing amide derivatives as antagonists of transforming growth factor-β (TGF-β)
INVENTOR(S): Maruyama, Yasufumi; Hirabayashi, Kazuko; Hori, Katsutoshi
PATENT ASSIGNEE(S): Nippon Shinyaku Co., Ltd., Japan
SOURCE: PCT Int. Appl., 123 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003037862	A1	20030508	WO 2002-JP11232	20021029
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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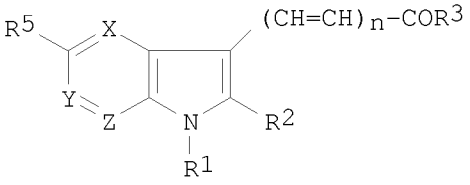
AU 2002344424	A1	20030512	AU 2002-344424	20021029
EP 1452525	A1	20040901	EP 2002-779936	20021029

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
US 20050014942 A1 20050120 US 2004-494622 20040430
PRIORITY APPLN. INFO.: JP 2001-332942 A 20011030
JP 2002-127771 A 20020430
WO 2002-JP11232 W 20021029
OTHER SOURCE(S): MARPAT 138:368914
GI



I

AB Amide derivs. represented by the general formula (I) or pharmaceutically acceptable salts thereof, and pharmaceutical compns. containing the same as the active ingredient [wherein n is 0 or 1; X = CR4, N; Y = CR6, N; Z = CR7, N; R1, R2 = H, optionally substituted alkyl, acyl, optionally substituted aryl, an optionally substituted aromatic heterocyclic group, or the like; R4, R5, R6, R7 = H, halogeno, hydroxyl, amino, alkyl, haloalkyl, alkoxy, monoalkylamino, dialkylamino, arylalkyl, cyano, nitro, or the like; R3 = optionally substituted alkylamino, optionally substituted arylamino, optionally substituted cyclic amino, or the like] are disclosed. The above compds. are useful as TGF-β antagonists for the treatment of pulmonary fibrosis, scleroderma, systemic scleroderma, and nephritis. Thus, 9.74 g 3-(1-methyl-2-phenyl-1H-pyrrolo[2,3-b]pyridin-3-yl)acrylic acid, 10.95 g 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride, and 7.1 g 1-hydroxybenzotriazole were mixed with 20 mL DMF, stirred at room temperature for 30 min, treated with 9.75 g salsolidine hydrochloride, and stirred at room temperature for 15 h to give, after workup and silica gel chromatog., 15.7 g 6,7-dimethoxy-1-methyl-2-[(2E)-3-(1-methyl-2-phenyl-1H-pyrrolo[2,3-b]pyridin-3-yl)-2-propenoyl]-1,2,3,4-tetrahydroisoquinoline hydrochloride (II). In an assay for inhibiting TGF-β-induced collagen production, II and 2-[(2E)-3-[1-methyl-2-(4-fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-3-yl]-2-propenoyl]-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline hydrochloride at 1 μM inhibited the uptake of [3H]proline in human normal fibroblast cell line (NHDF) by 65 and 140%, resp., when the difference between the uptake of [3H]proline in the absence of TGF-β and that in the presence of TGF-β was set at 100%. Pharmaceutical formulations, e.g. a tablet containing II, were described.

IT 521983-46-0P 521983-47-1P 521983-48-2P
521983-49-3P 521983-51-7P 521983-52-8P
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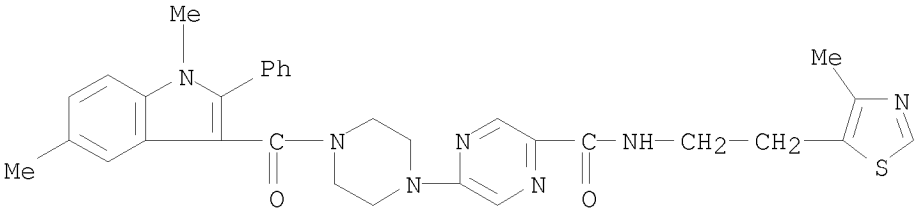
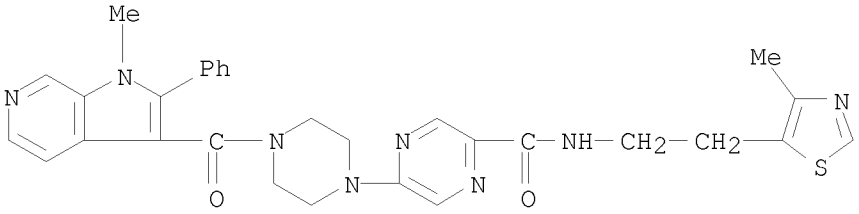
521984-89-4P 521984-90-7P 521985-46-6P
521985-47-7P 521985-48-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of indole- and pyrrolo[2,3-b]pyridine-containing amide derivs. as
antagonists of transforming growth factor-β for treatment of pulmonary fibrosis, scleroderma, systemic scleroderma, and nephritis)

RN 521983-46-0 CAPLUS
CN Pyrazinecarboxamide, 5-[4-[(1,5-dimethyl-2-phenyl-1H-indol-3-yl)carbonyl]-1-piperazinyl]-N-[2-(4-methyl-5-thiazolyl)ethyl]-, trihydrochloride (9CI) (CA INDEX NAME)



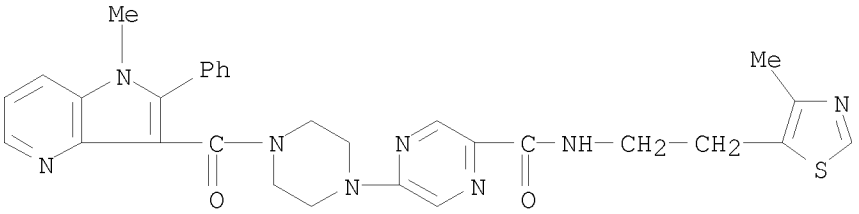
●3 HCl

RN 521983-47-1 CAPLUS
CN Pyrazinecarboxamide, 5-[4-[(1-methyl-2-phenyl-1H-pyrrolo[2,3-c]pyridin-3-yl)carbonyl]-1-piperazinyl]-N-[2-(4-methyl-5-thiazolyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

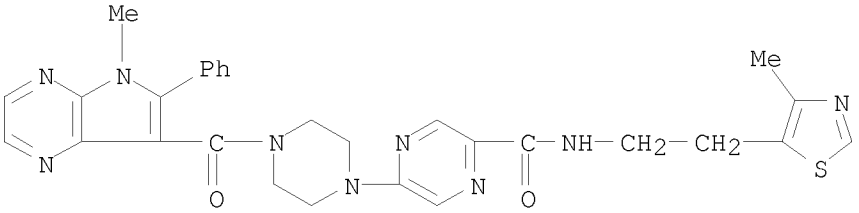


●2 HCl

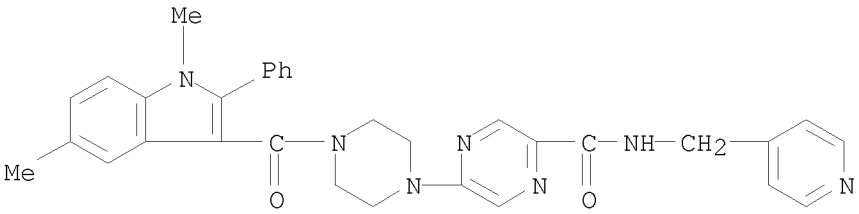
RN 521983-48-2 CAPLUS
CN Pyrazinecarboxamide, 5-[4-[(1-methyl-2-phenyl-1H-pyrrolo[3,2-b]pyridin-3-yl)carbonyl]-1-piperazinyl]-N-[2-(4-methyl-5-thiazolyl)ethyl]- (9CI) (CA INDEX NAME)



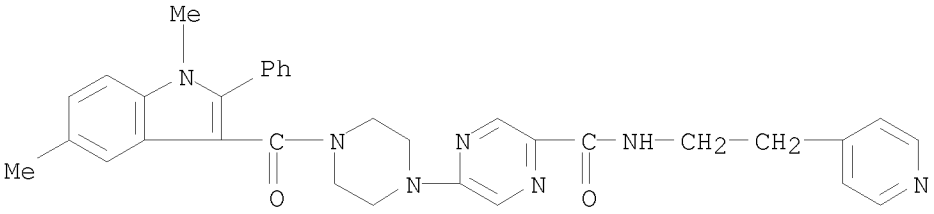
RN 521983-49-3 CAPLUS
CN Pyrazinecarboxamide, 5-[4-[(5-methyl-6-phenyl-5H-pyrrolo[2,3-b]pyrazin-7-yl)carbonyl]-1-piperazinyl]-N-[2-(4-methyl-5-thiazolyl)ethyl]- (9CI) (CA INDEX NAME)



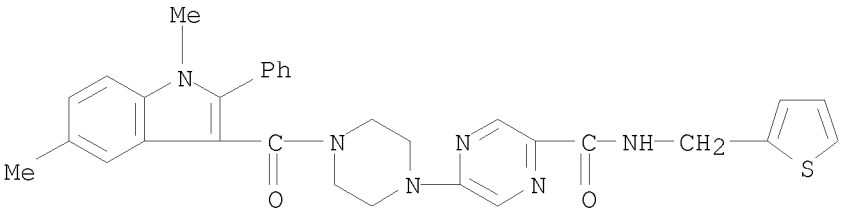
RN 521983-51-7 CAPLUS
CN Pyrazinecarboxamide, 5-[4-[(1,5-dimethyl-2-phenyl-1H-indol-3-yl)carbonyl]-1-piperazinyl]-N-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



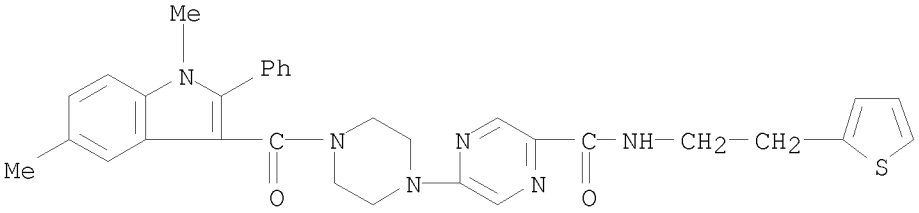
RN 521983-52-8 CAPLUS
CN Pyrazinecarboxamide, 5-[4-[(1,5-dimethyl-2-phenyl-1H-indol-3-yl)carbonyl]-1-piperazinyl]-N-[2-(4-pyridinyl)ethyl]- (9CI) (CA INDEX NAME)



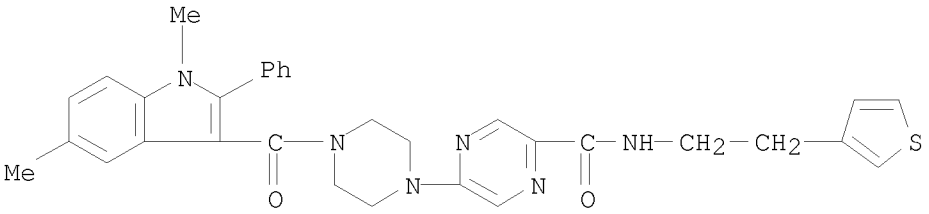
RN 521983-53-9 CAPLUS
CN Pyrazinecarboxamide, 5-[4-[(1,5-dimethyl-2-phenyl-1H-indol-3-yl)carbonyl]-1-piperazinyl]-N-(2-thienylmethyl)- (9CI) (CA INDEX NAME)



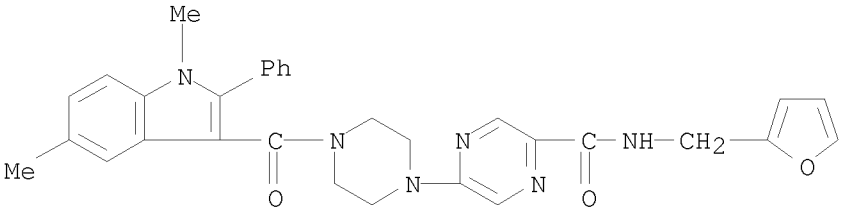
RN 521983-54-0 CAPLUS
CN Pyrazinecarboxamide, 5-[4-[(1,5-dimethyl-2-phenyl-1H-indol-3-yl)carbonyl]-1-piperazinyl]-N-[2-(2-thienyl)ethyl]- (9CI) (CA INDEX NAME)



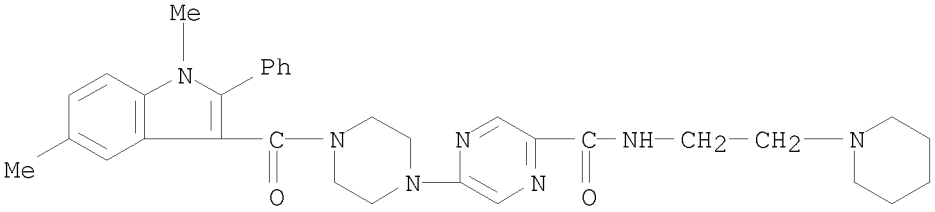
RN 521983-55-1 CAPLUS
CN Pyrazinecarboxamide, 5-[4-[(1,5-dimethyl-2-phenyl-1H-indol-3-yl)carbonyl]-1-piperazinyl]-N-[2-(3-thienyl)ethyl]- (9CI) (CA INDEX NAME)



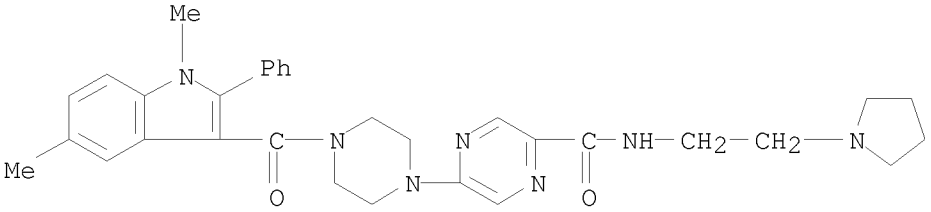
RN 521983-56-2 CAPLUS
CN Pyrazinecarboxamide, 5-[4-[(1,5-dimethyl-2-phenyl-1H-indol-3-yl)carbonyl]-1-piperazinyl]-N-(2-furanylmethyl)- (9CI) (CA INDEX NAME)



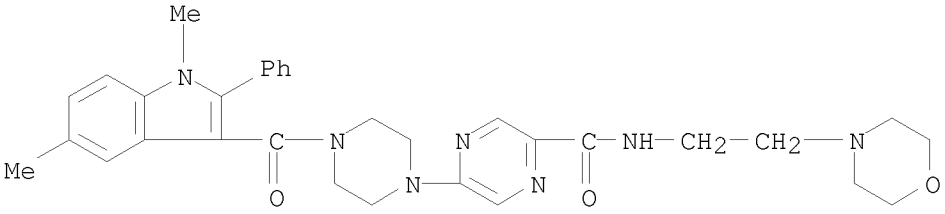
RN 521983-57-3 CAPLUS
CN Pyrazinecarboxamide, 5-[4-[(1,5-dimethyl-2-phenyl-1H-indol-3-yl)carbonyl]-1-piperazinyl]-N-[2-(1-piperidinyl)ethyl]- (9CI) (CA INDEX NAME)



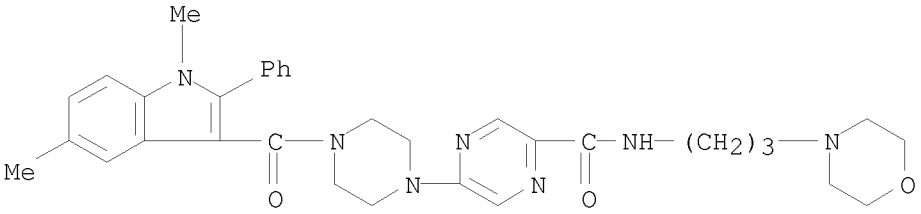
RN 521983-58-4 CAPLUS
CN Pyrazinecarboxamide, 5-[4-[(1,5-dimethyl-2-phenyl-1H-indol-3-yl)carbonyl]-1-piperazinyl]-N-[2-(1-pyrrolidinyl)ethyl]- (9CI) (CA INDEX NAME)



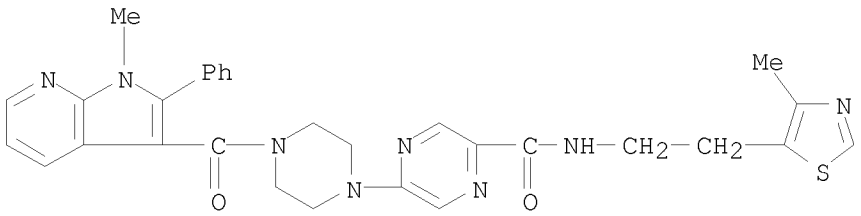
RN 521983-59-5 CAPLUS
CN Pyrazinecarboxamide, 5-[4-[(1,5-dimethyl-2-phenyl-1H-indol-3-yl)carbonyl]-1-piperazinyl]-N-[2-(4-morpholinyl)ethyl]- (9CI) (CA INDEX NAME)



RN 521983-60-8 CAPLUS
CN Pyrazinecarboxamide, 5-[4-[(1,5-dimethyl-2-phenyl-1H-indol-3-yl)carbonyl]-1-piperazinyl]-N-[3-(4-morpholinyl)propyl]- (9CI) (CA INDEX NAME)

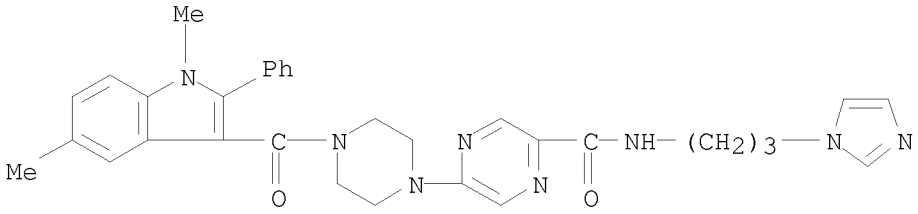


RN 521983-68-6 CAPLUS
CN Pyrazinecarboxamide, 5-[4-[(1-methyl-2-phenyl-1H-pyrrolo[2,3-b]pyridin-3-yl)carbonyl]-1-piperazinyl]-N-[2-(4-methyl-5-thiazolyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

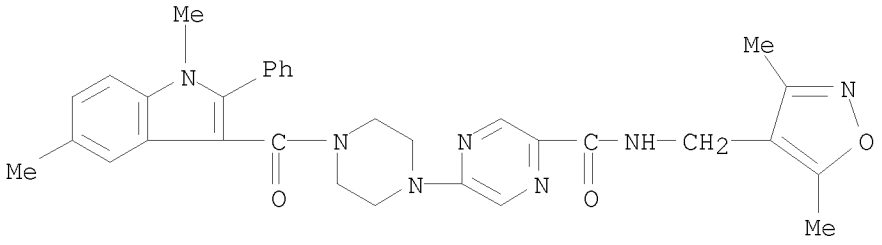


● 2 HCl

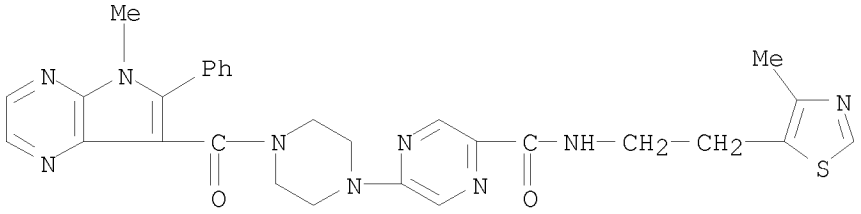
RN 521983-72-2 CAPLUS
CN Pyrazinecarboxamide, 5-[4-[(1,5-dimethyl-2-phenyl-1H-indol-3-yl)carbonyl]-1-piperazinyl]-N-[3-(1H-imidazol-1-yl)propyl]- (9CI) (CA INDEX NAME)



RN 521983-73-3 CAPLUS
CN Pyrazinecarboxamide, N-[(3,5-dimethyl-4-isoxazolyl)methyl]-5-[4-[(1,5-dimethyl-2-phenyl-1H-indol-3-yl)carbonyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)

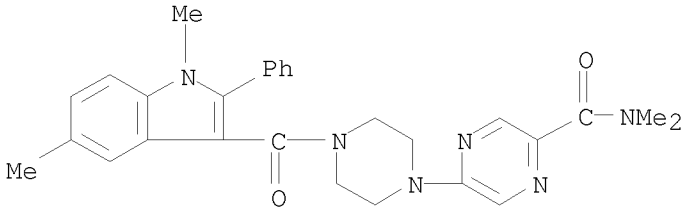


RN 521983-90-4 CAPLUS
CN Pyrazinecarboxamide, 5-[4-[(5-methyl-6-phenyl-5H-pyrrolo[2,3-b]pyrazin-7-yl)carbonyl]-1-piperazinyl]-N-[2-(4-methyl-5-thiazolyl)ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

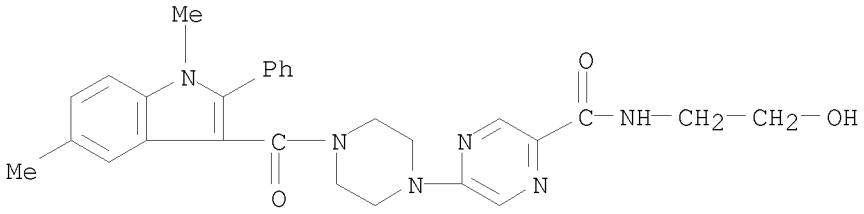


● HCl

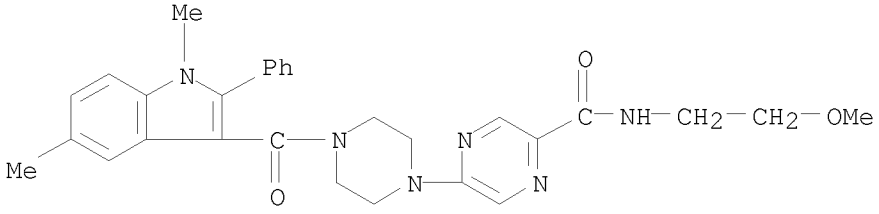
RN 521984-04-3 CAPLUS
CN Pyrazinecarboxamide, 5-[4-[(1,5-dimethyl-2-phenyl-1H-indol-3-yl)carbonyl]-1-piperazinyl]-N,N-dimethyl- (9CI) (CA INDEX NAME)



RN 521984-05-4 CAPLUS
CN Pyrazinecarboxamide, 5-[4-[(1,5-dimethyl-2-phenyl-1H-indol-3-yl)carbonyl]-1-piperazinyl]-N-(2-hydroxyethyl)- (9CI) (CA INDEX NAME)

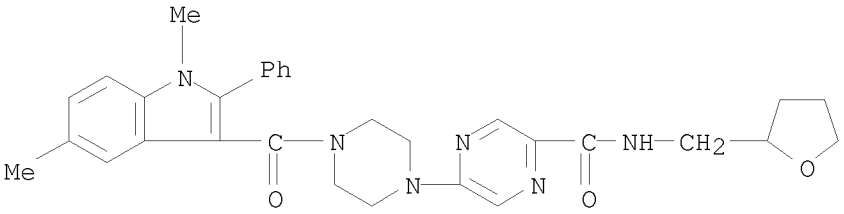


RN 521984-06-5 CAPLUS
CN Pyrazinecarboxamide, 5-[4-[(1,5-dimethyl-2-phenyl-1H-indol-3-yl)carbonyl]-1-piperazinyl]-N-(2-methoxyethyl)- (9CI) (CA INDEX NAME)

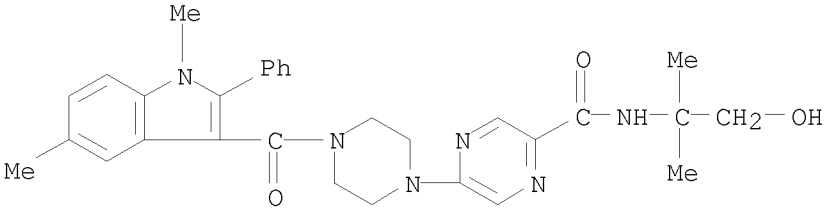


RN 521984-07-6 CAPLUS
CN Pyrazinecarboxamide, 5-[4-[(1,5-dimethyl-2-phenyl-1H-indol-3-yl)carbonyl]-

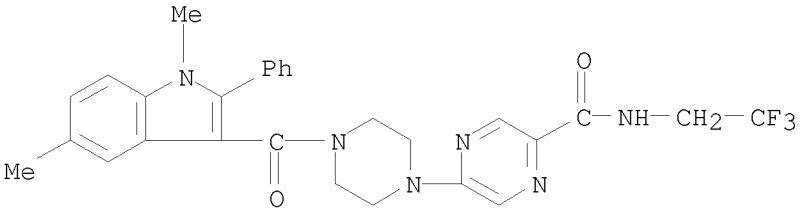
1-piperazinyl]-N-[(tetrahydro-2-furanyl)methyl]- (9CI) (CA INDEX NAME)



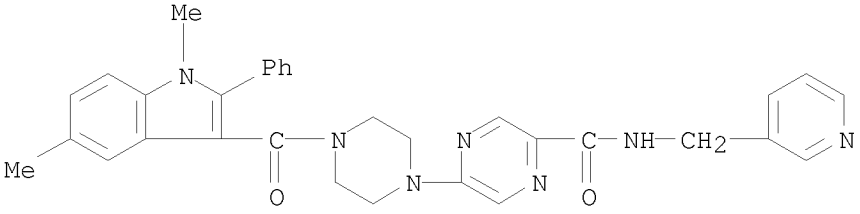
RN 521984-08-7 CAPLUS
CN Pyrazinecarboxamide, 5-[4-[(1,5-dimethyl-2-phenyl-1H-indol-3-yl)carbonyl]-
1-piperazinyl]-N-(2-hydroxy-1,1-dimethylethyl)- (9CI) (CA INDEX NAME)



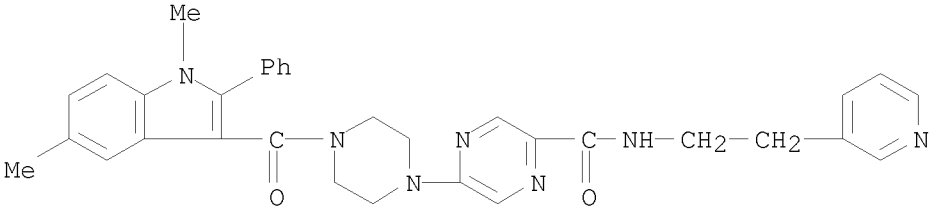
RN 521984-10-1 CAPLUS
CN Pyrazinecarboxamide, 5-[4-[(1,5-dimethyl-2-phenyl-1H-indol-3-yl)carbonyl]-
1-piperazinyl]-N-(2,2,2-trifluoroethyl)- (9CI) (CA INDEX NAME)



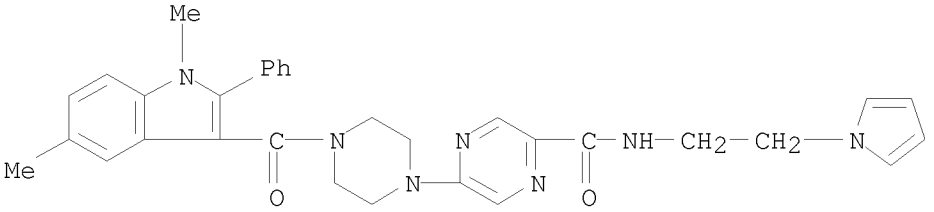
RN 521984-12-3 CAPLUS
CN Pyrazinecarboxamide, 5-[4-[(1,5-dimethyl-2-phenyl-1H-indol-3-yl)carbonyl]-
1-piperazinyl]-N-(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)



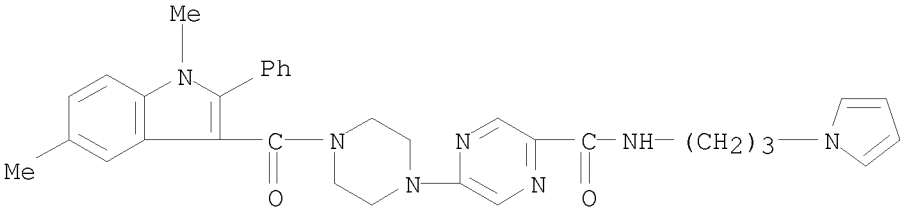
RN 521984-13-4 CAPLUS
CN Pyrazinecarboxamide, 5-[4-[(1,5-dimethyl-2-phenyl-1H-indol-3-yl)carbonyl]-
1-piperazinyl]-N-[2-(3-pyridinyl)ethyl]- (9CI) (CA INDEX NAME)



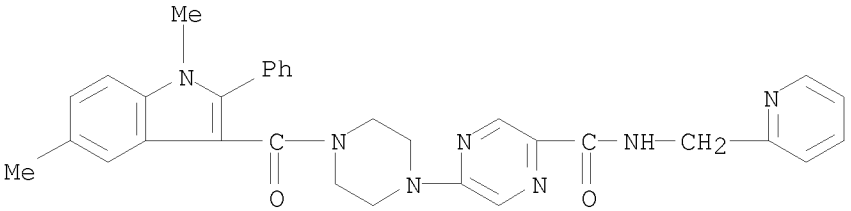
RN 521984-14-5 CAPLUS
CN Pyrazinecarboxamide, 5-[4-[(1,5-dimethyl-2-phenyl-1H-indol-3-yl)carbonyl]-1-piperazinyl]-N-[2-(1H-pyrrol-1-yl)ethyl]- (9CI) (CA INDEX NAME)



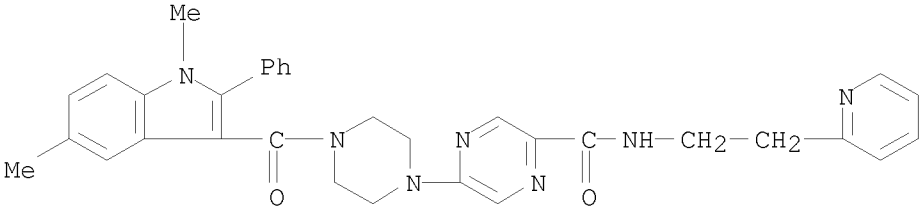
RN 521984-15-6 CAPLUS
CN Pyrazinecarboxamide, 5-[4-[(1,5-dimethyl-2-phenyl-1H-indol-3-yl)carbonyl]-1-piperazinyl]-N-[3-(1H-pyrrol-1-yl)propyl]- (9CI) (CA INDEX NAME)



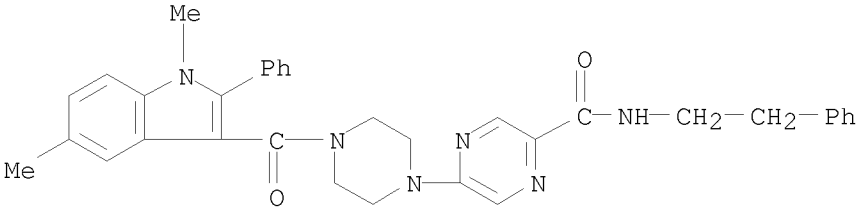
RN 521984-16-7 CAPLUS
CN Pyrazinecarboxamide, 5-[4-[(1,5-dimethyl-2-phenyl-1H-indol-3-yl)carbonyl]-1-piperazinyl]-N-(2-pyridinylmethyl)- (9CI) (CA INDEX NAME)



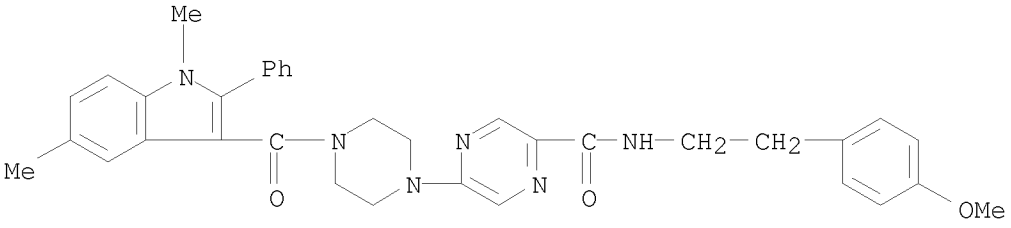
RN 521984-17-8 CAPLUS
CN Pyrazinecarboxamide, 5-[4-[(1,5-dimethyl-2-phenyl-1H-indol-3-yl)carbonyl]-1-piperazinyl]-N-[2-(2-pyridinyl)ethyl]- (9CI) (CA INDEX NAME)



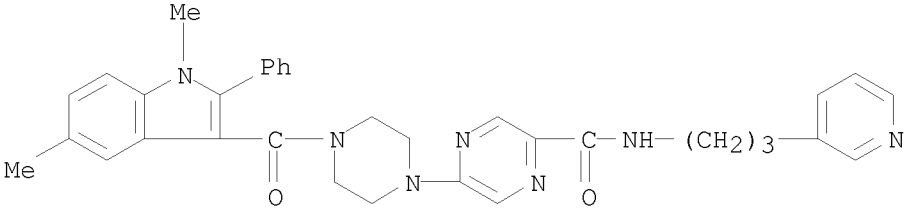
RN 521984-18-9 CAPLUS
CN Pyrazinecarboxamide, 5-[4-[(1,5-dimethyl-2-phenyl-1H-indol-3-yl)carbonyl]-1-piperazinyl]-N-(2-phenylethyl)- (9CI) (CA INDEX NAME)



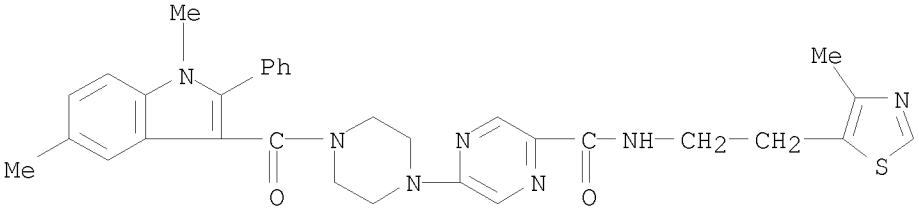
RN 521984-19-0 CAPLUS
CN Pyrazinecarboxamide, 5-[4-[(1,5-dimethyl-2-phenyl-1H-indol-3-yl)carbonyl]-1-piperazinyl]-N-[2-(4-methoxyphenyl)ethyl]- (9CI) (CA INDEX NAME)



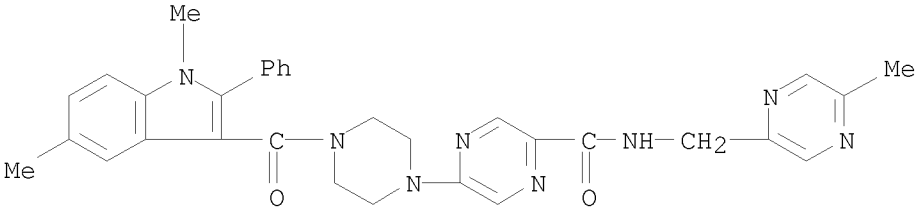
RN 521984-20-3 CAPLUS
CN Pyrazinecarboxamide, 5-[4-[(1,5-dimethyl-2-phenyl-1H-indol-3-yl)carbonyl]-1-piperazinyl]-N-[3-(3-pyridinyl)propyl]- (9CI) (CA INDEX NAME)



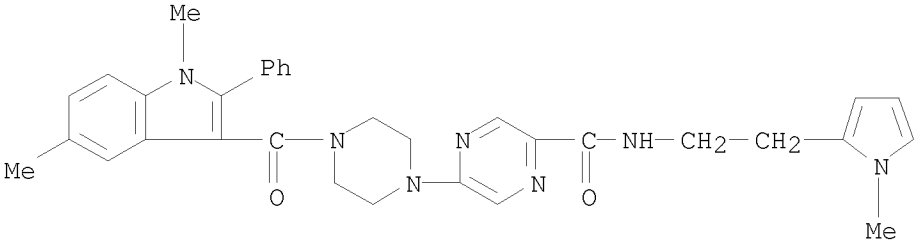
RN 521984-21-4 CAPLUS
CN Pyrazinecarboxamide, 5-[4-[(1,5-dimethyl-2-phenyl-1H-indol-3-yl)carbonyl]-1-piperazinyl]-N-[2-(4-methyl-5-thiazolyl)ethyl]- (9CI) (CA INDEX NAME)



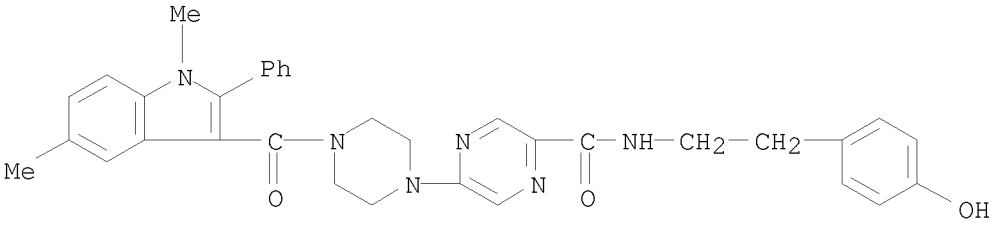
RN 521984-22-5 CAPLUS
CN Pyrazinecarboxamide, 5-[4-[(1,5-dimethyl-2-phenyl-1H-indol-3-yl)carbonyl]-1-piperazinyl]-N-[(5-methylpyrazinyl)methyl]- (9CI) (CA INDEX NAME)



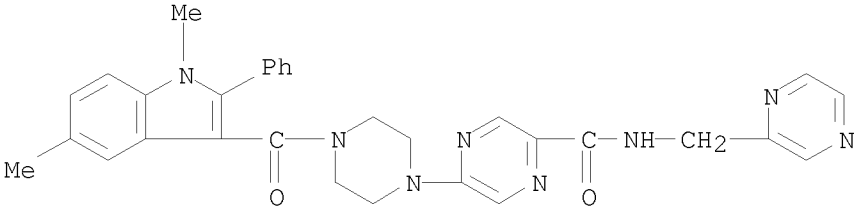
RN 521984-23-6 CAPLUS
CN Pyrazinecarboxamide, 5-[4-[(1,5-dimethyl-2-phenyl-1H-indol-3-yl)carbonyl]-1-piperazinyl]-N-[2-(1-methyl-1H-pyrrol-2-yl)ethyl]- (9CI) (CA INDEX NAME)



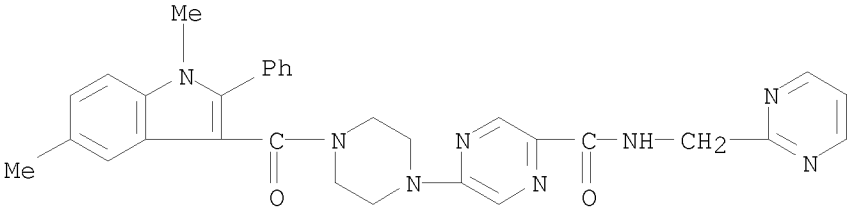
RN 521984-24-7 CAPLUS
CN Pyrazinecarboxamide, 5-[4-[(1,5-dimethyl-2-phenyl-1H-indol-3-yl)carbonyl]-1-piperazinyl]-N-[2-(4-hydroxyphenyl)ethyl]- (9CI) (CA INDEX NAME)



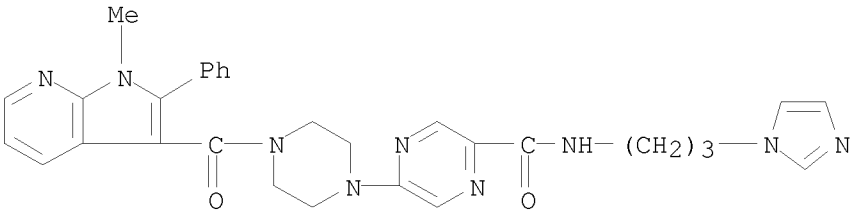
RN 521984-25-8 CAPLUS
CN Pyrazinecarboxamide, 5-[4-[(1,5-dimethyl-2-phenyl-1H-indol-3-yl)carbonyl]-1-piperazinyl]-N-(pyrazinylmethyl)- (9CI) (CA INDEX NAME)



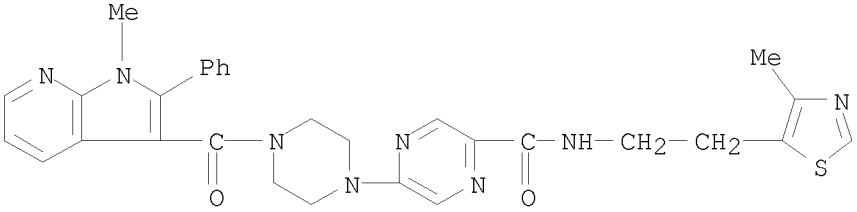
RN 521984-26-9 CAPLUS
CN Pyrazinecarboxamide, 5-[4-[(1,5-dimethyl-2-phenyl-1H-indol-3-yl)carbonyl]-1-piperazinyl]-N-(2-pyrimidinylmethyl)- (9CI) (CA INDEX NAME)



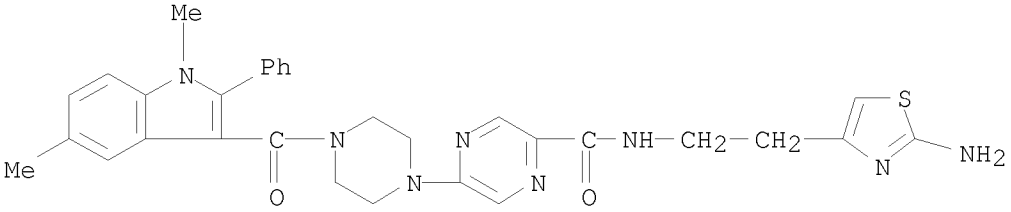
RN 521984-27-0 CAPLUS
CN Pyrazinecarboxamide, N-[3-(1H-imidazol-1-yl)propyl]-5-[4-[(1-methyl-2-phenyl-1H-pyrrolo[2,3-b]pyridin-3-yl)carbonyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)



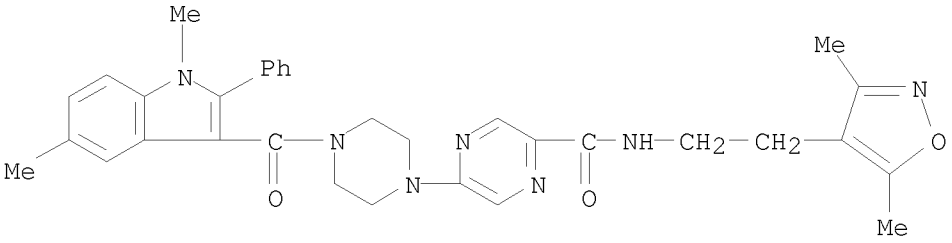
RN 521984-28-1 CAPLUS
CN Pyrazinecarboxamide, 5-[4-[(1-methyl-2-phenyl-1H-pyrrolo[2,3-b]pyridin-3-yl)carbonyl]-1-piperazinyl]-N-[2-(4-methyl-5-thiazolyl)ethyl]- (9CI) (CA INDEX NAME)



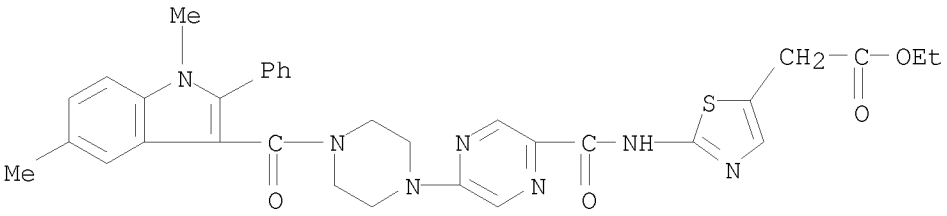
RN 521984-29-2 CAPLUS
CN Pyrazinecarboxamide, N-[2-(2-amino-4-thiazolyl)ethyl]-5-[4-[(1,5-dimethyl-2-phenyl-1H-indol-3-yl)carbonyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)



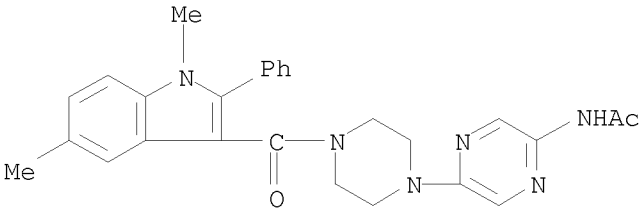
RN 521984-30-5 CAPLUS
CN Pyrazinecarboxamide, N-[2-(3,5-dimethyl-4-isoxazolyl)ethyl]-5-[4-[(1,5-dimethyl-2-phenyl-1H-indol-3-yl)carbonyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)



RN 521984-31-6 CAPLUS
CN 5-Thiazoleacetic acid, 2-[[[5-[4-[(1,5-dimethyl-2-phenyl-1H-indol-3-yl)carbonyl]-1-piperazinyl]pyrazinyl]carbonyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)

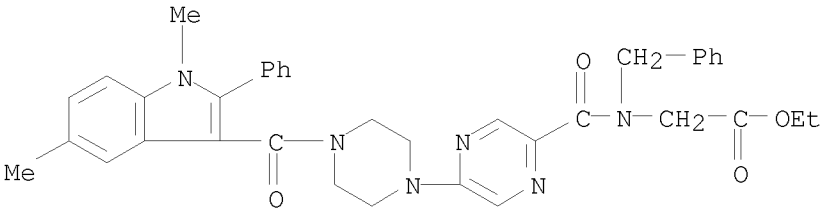


RN 521984-60-1 CAPLUS
CN Acetamide, N-[5-[4-[(1,5-dimethyl-2-phenyl-1H-indol-3-yl)carbonyl]-1-piperazinyl]pyrazinyl]- (9CI) (CA INDEX NAME)

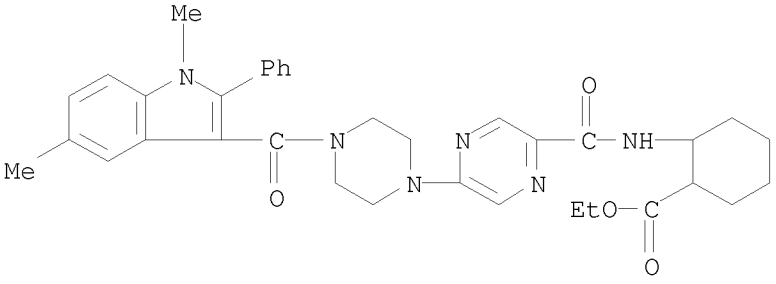


RN 521984-64-5 CAPLUS
CN Glycine, N-[[5-[4-[(1,5-dimethyl-2-phenyl-1H-indol-3-yl)carbonyl]-1-piperazinyl]pyrazinyl]carbonyl]-N-(phenylmethyl)-, ethyl ester (9CI) (CA

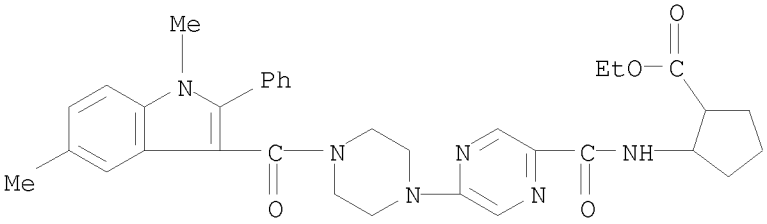
INDEX NAME)



RN 521984-66-7 CAPLUS
CN Cyclohexanecarboxylic acid, 2-[[[5-[4-[(1,5-dimethyl-2-phenyl-1H-indol-3-yl)carbonyl]-1-piperazinyl]pyrazinyl]carbonyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)

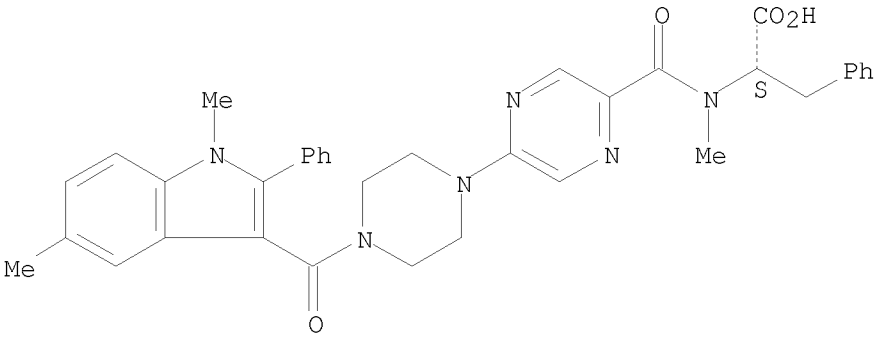


RN 521984-68-9 CAPLUS
CN Cyclopentanecarboxylic acid, 2-[[[5-[4-[(1,5-dimethyl-2-phenyl-1H-indol-3-yl)carbonyl]-1-piperazinyl]pyrazinyl]carbonyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)

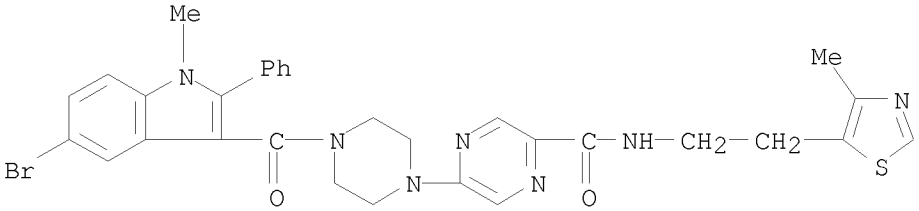


RN 521984-71-4 CAPLUS
CN L-Phenylalanine, N-[[5-[4-[(1,5-dimethyl-2-phenyl-1H-indol-3-yl)carbonyl]-1-piperazinyl]pyrazinyl]carbonyl]-N-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

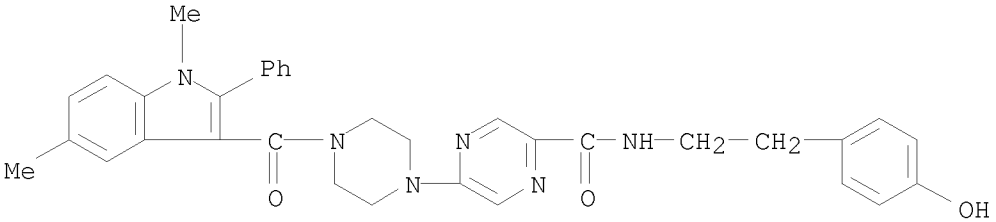


RN 521984-82-7 CAPLUS
CN Pyrazinecarboxamide, 5-[4-[(5-bromo-1-methyl-2-phenyl-1H-indol-3-yl)carbonyl]-1-piperazinyl]-N-[2-(4-methyl-5-thiazolyl)ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



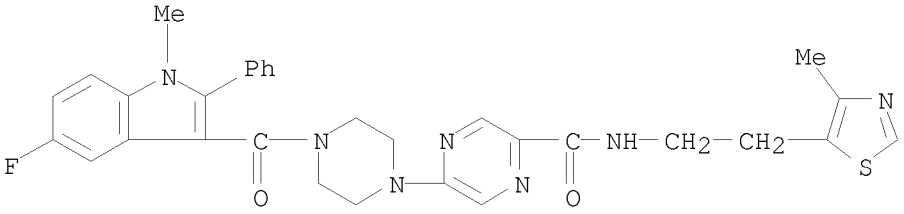
● HCl

RN 521984-83-8 CAPLUS
CN Pyrazinecarboxamide, 5-[4-[(1,5-dimethyl-2-phenyl-1H-indol-3-yl)carbonyl]-1-piperazinyl]-N-[2-(4-hydroxyphenyl)ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



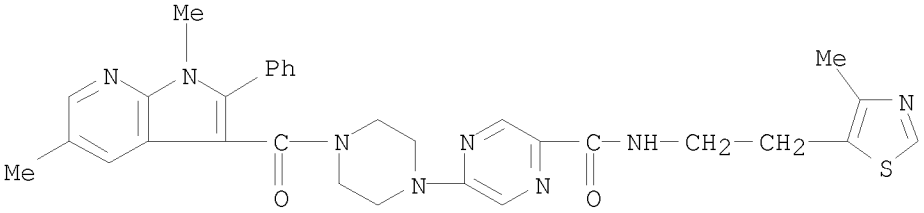
● HCl

RN 521984-85-0 CAPLUS
CN Pyrazinecarboxamide, 5-[4-[(5-fluoro-1-methyl-2-phenyl-1H-indol-3-yl)carbonyl]-1-piperazinyl]-N-[2-(4-methyl-5-thiazolyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



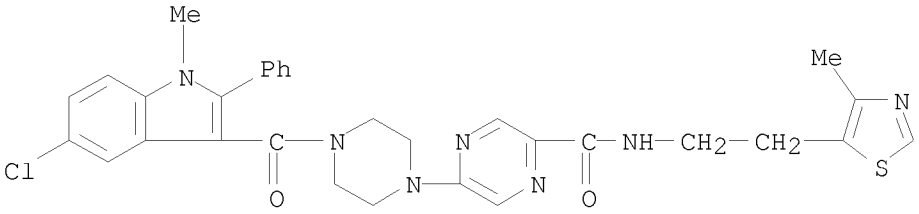
●2 HCl

RN 521984-86-1 CAPLUS
CN Pyrazinecarboxamide, 5-[4-[(1,5-dimethyl-2-phenyl-1H-pyrrolo[2,3-b]pyridin-3-yl)carbonyl]-1-piperazinyl]-N-[2-(4-methyl-5-thiazolyl)ethyl]-, trihydrochloride (9CI) (CA INDEX NAME)



●3 HCl

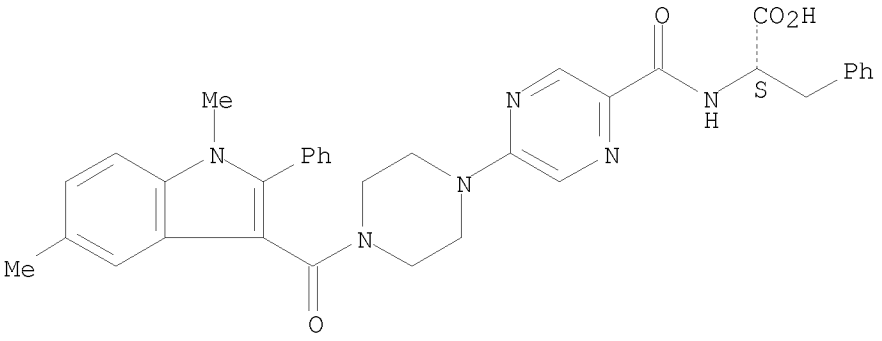
RN 521984-88-3 CAPLUS
CN Pyrazinecarboxamide, 5-[4-[(5-chloro-1-methyl-2-phenyl-1H-indol-3-yl)carbonyl]-1-piperazinyl]-N-[2-(4-methyl-5-thiazolyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

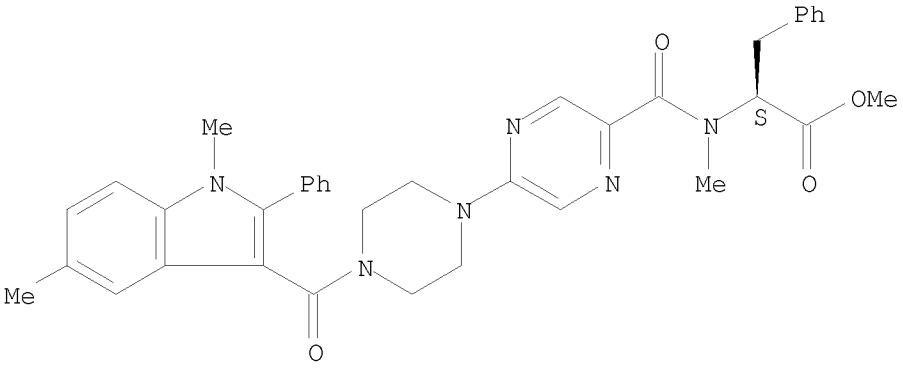
RN 521984-89-4 CAPLUS
CN L-Phenylalanine, N-[[5-[4-[(1,5-dimethyl-2-phenyl-1H-indol-3-yl)carbonyl]-1-piperazinyl]pyrazinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

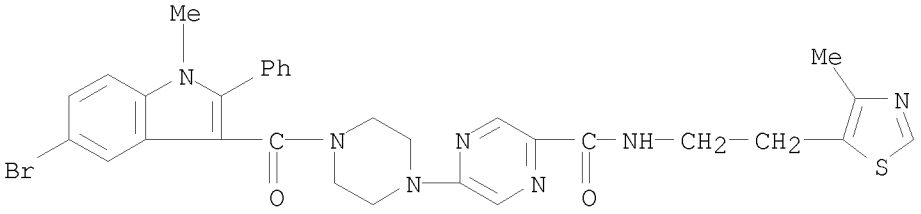


RN 521984-90-7 CAPLUS
CN L-Phenylalanine, N-[[5-[4-[(1,5-dimethyl-2-phenyl-1H-indol-3-yl)carbonyl]-1-piperazinyl]pyrazinyl]carbonyl]-N-methyl-, methyl ester (9CI) (CA INDEX NAME)

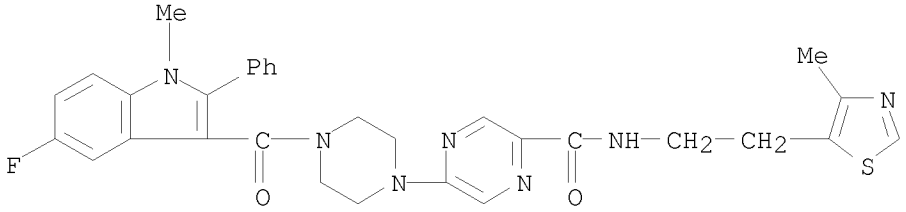
Absolute stereochemistry.



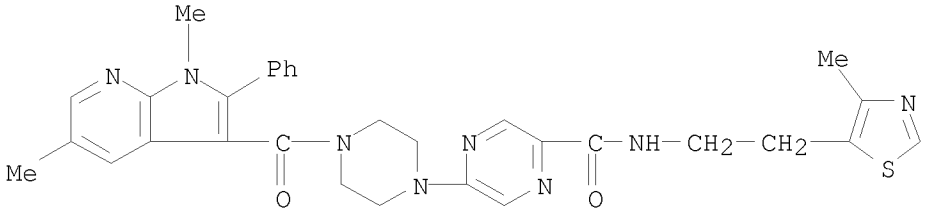
RN 521985-46-6 CAPLUS
CN Pyrazinecarboxamide, 5-[4-[(5-bromo-1-methyl-2-phenyl-1H-indol-3-yl)carbonyl]-1-piperazinyl]-N-[2-(4-methyl-5-thiazolyl)ethyl]- (9CI) (CA INDEX NAME)



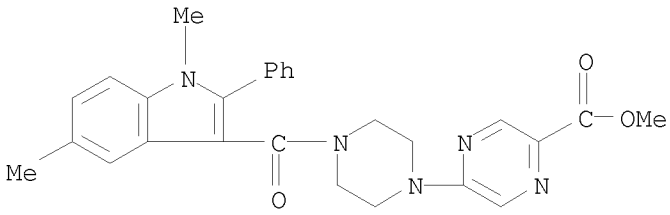
RN 521985-47-7 CAPLUS
CN Pyrazinecarboxamide, 5-[4-[(5-fluoro-1-methyl-2-phenyl-1H-indol-3-yl)carbonyl]-1-piperazinyl]-N-[2-(4-methyl-5-thiazolyl)ethyl]- (9CI) (CA INDEX NAME)



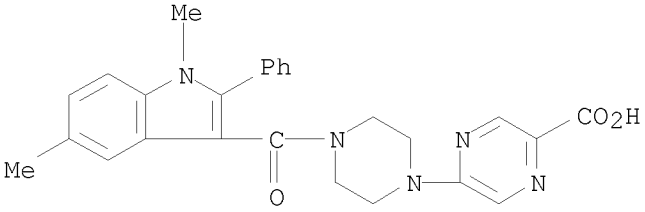
RN 521985-48-8 CAPLUS
CN Pyrazinecarboxamide, 5-[4-[(1,5-dimethyl-2-phenyl-1H-pyrrolo[2,3-b]pyridin-3-yl)carbonyl]-1-piperazinyl]-N-[2-(4-methyl-5-thiazolyl)ethyl]- (9CI) (CA INDEX NAME)



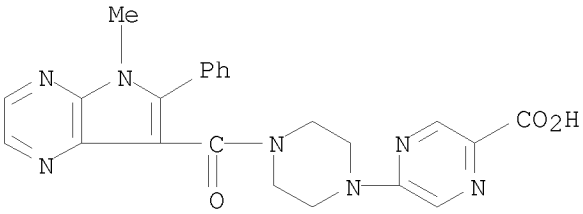
IT 521985-04-6P 521985-05-7P 521985-07-9P
521985-08-0P 521985-14-8P 521985-15-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of indole- and pyrrolo[2,3-b]pyridine-containing amide derivs. as
antagonists of transforming growth factor-β for treatment of
pulmonary fibrosis, scleroderma, systemic scleroderma, and nephritis)
RN 521985-04-6 CAPLUS
CN Pyrazinecarboxylic acid, 5-[4-[(1,5-dimethyl-2-phenyl-1H-indol-3-yl)carbonyl]-1-piperazinyl]-, methyl ester (9CI) (CA INDEX NAME)



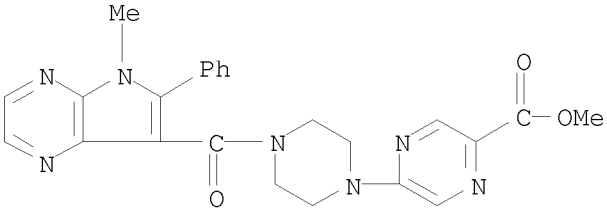
RN 521985-05-7 CAPLUS
CN Pyrazinecarboxylic acid, 5-[4-[(1,5-dimethyl-2-phenyl-1H-indol-3-yl)carbonyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)



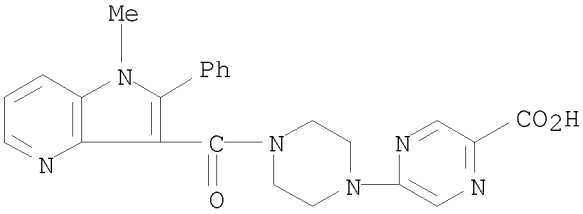
RN 521985-07-9 CAPLUS
CN Pyrazinecarboxylic acid, 5-[4-[(5-methyl-6-phenyl-5H-pyrrolo[2,3-b]pyrazin-7-yl)carbonyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)



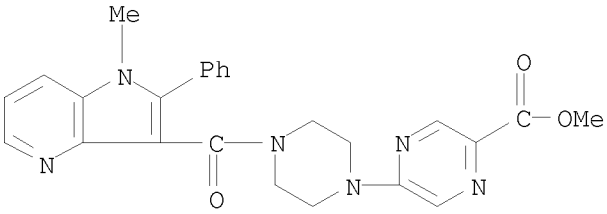
RN 521985-08-0 CAPLUS
CN Pyrazinecarboxylic acid, 5-[4-[(5-methyl-6-phenyl-5H-pyrrolo[2,3-b]pyrazin-7-yl)carbonyl]-1-piperazinyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 521985-14-8 CAPLUS
CN Pyrazinecarboxylic acid, 5-[4-[(1-methyl-2-phenyl-1H-pyrrolo[3,2-b]pyridin-3-yl)carbonyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)



RN 521985-15-9 CAPLUS
CN Pyrazinecarboxylic acid, 5-[4-[(1-methyl-2-phenyl-1H-pyrrolo[3,2-b]pyridin-3-yl)carbonyl]-1-piperazinyl]-, methyl ester (9CI) (CA INDEX NAME)



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SESSION RESUMED IN FILE 'CAPLUS' AT 13:09:53 ON 20 MAY 2008
FILE 'CAPLUS' ENTERED AT 13:09:53 ON 20 MAY 2008
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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	52.41	231.82

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-4.00	-4.00

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(FILE 'HOME' ENTERED AT 12:59:50 ON 20 MAY 2008)

FILE 'REGISTRY' ENTERED AT 13:02:47 ON 20 MAY 2008
L1 STRUCTURE UPLOADED
L2 18 S L1
L3 366 S L1 SSS FULL

FILE 'CAPLUS' ENTERED AT 13:03:28 ON 20 MAY 2008
L4 10 S L2
L5 41 S L3

=> d 21-21

L5 ANSWER 21 OF 41 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2003:5937 CAPLUS
DN 138:73273
TI Preparation of [1,2']bipyrazinyl 5-HT2 receptor ligands for treatment of sexual dysfunction
IN Chiang, Yuan-Ching Phoebe; Dasilva-Jardine, Paul Andrew; Garigipati, Ravi S.; Guzman-Perez, Angel; Novomisle, William Albert; Welch, Willard Mckowan
PA Pfizer Products Inc., USA
SO PCT Int. Appl., 151 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003000666	A1	20030103	WO 2002-IB2293	20020617
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
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	US 20030105106	A1	20030605	US 2002-156884	20020528
	US 6825198	B2	20041130		
	US 20030125334	A1	20030703	US 2002-163881	20020605
	US 6894050	B2	20050517		
	CA 2455292	A1	20030103	CA 2002-2455292	20020617
	AU 2002309183	A1	20030108	AU 2002-309183	20020617
	NZ 529542	A	20031219	NZ 2002-529542	20020617
	NZ 529543	A	20031219	NZ 2002-529543	20020617
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	HU 2004000251	A2	20040830	HU 2004-251	20020617
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	JP 2005501821	T	20050120	JP 2003-507071	20020617
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	IN 2003MN01057	A	20051021	IN 2003-MN1057	20031118
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	US 20050090503	A1	20050428	US 2004-922058	20040819
	US 20050032809	A1	20050210	US 2004-942345	20040916
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	US 2002-156884	A3	20020528		
	US 2002-163881	A3	20020605		
	WO 2002-IB2293	W	20020617		

OS MARPAT 138:73273
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d l5 21-41 ibib abs hitstr

L5 ANSWER 21 OF 41 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:5937 CAPLUS
DOCUMENT NUMBER: 138:73273
TITLE: Preparation of [1,2']bipyrazinyl 5-HT2 receptor ligands for treatment of sexual dysfunction
INVENTOR(S): Chiang, Yuan-Ching Phoebe; Dasilva-Jardine, Paul Andrew; Garigipati, Ravi S.; Guzman-Perez, Angel; Novomisle, William Albert; Welch, Willard Mckowan
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 151 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003000666	A1	20030103	WO 2002-IB2293		20020617
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW					
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US 6825198	B2	20041130			
US 20030125334	A1	20030703	US 2002-163881		20020605
US 6894050	B2	20050517			
CA 2455292	A1	20030103	CA 2002-2455292		20020617
AU 2002309183	A1	20030108	AU 2002-309183		20020617
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EP 1401820	A1	20040331	EP 2002-735869		20020617
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
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BR 2002010471	A	20040810	BR 2002-10471		20020617
HU 2004000251	A2	20040830	HU 2004-251		20020617
HU 2004000251	A3	20060228			
JP 2005501821	T	20050120	JP 2003-507071		20020617
CN 1630645	A	20050622	CN 2002-813734		20020617
CN 1745074	A	20060308	CN 2002-812554		20020617
ZA 2003008842	A	20041123	ZA 2003-8842		20031113
ZA 2003008843	A	20041123	ZA 2003-8843		20031113
IN 2003MN01057	A	20051021	IN 2003-MN1057		20031118
MX 2003PA11941	A	20040326	MX 2003-PA11941		20031218
BG 108491	A	20050131	BG 2003-108491		20031222
US 20050020604	A1	20050127	US 2004-922198		20040819
US 20050090503	A1	20050428	US 2004-922058		20040819
US 20050032809	A1	20050210	US 2004-942345		20040916
US 6995159	B2	20060207			
US 20050054656	A1	20050310	US 2004-942346		20040916
PRIORITY APPLN. INFO.:			US 2001-299953P	P	20010621

US 2002-156884	A3	20020528
US 2002-163881	A3	20020605
WO 2002-IB2293	W	20020617

OTHER SOURCE(S): MARPAT 138:73273

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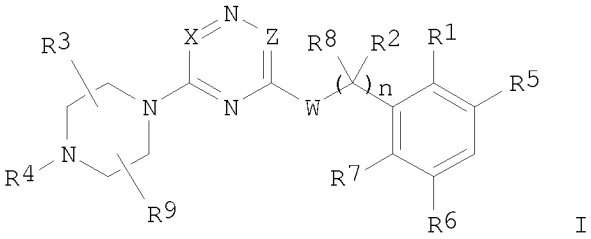

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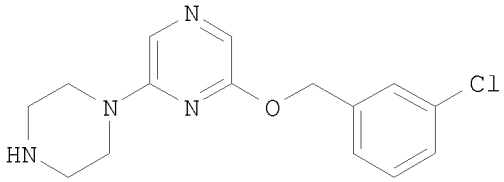


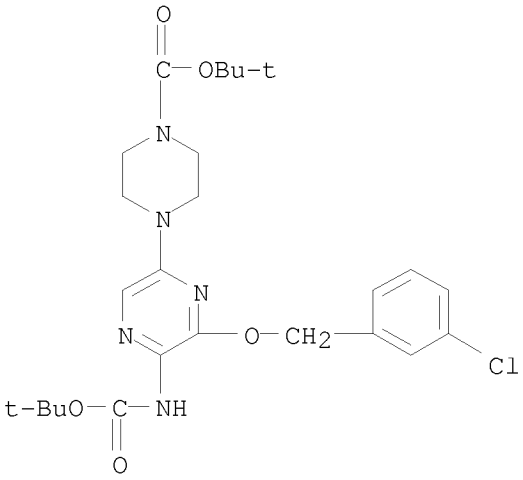
II

AB Title compds. (I) [wherein X and Z = independently CR; R = H, halo, alkyl(amino), or amino; W = O, S, NH, alkylamino, or acetylamino; at least one of R1, R5, R6, or R7 = independently halo, NO2, (alkyl)amino, CN, CONH2, (halo)alkyl, or alkoxy; or C2R1R5 = 5- or 6-membered aromatic or fused ring; or R1 taken together with R2 or R8 forms a 5- or 6-membered fused ring; R2 and R8 = independently H or (cyclo)alkyl; n = 0-2; R3 and R9 = independently H, halo, alkyl, or alkyl substituted with OH, F, or alkoxy; R4 = H, OH, (hydroxy)alkyl, cyanoalkyl, alkylcarbonyl, alkoxy(carbonyl), or alkenyl; or N-oxides, prodrugs, pharmaceutically acceptable salts, solvates, or hydrates thereof] were prepared as 5-hydroxytryptamine (5-HT) receptor ligands, in particular 5-HT2C receptor ligands. For instance, 2,6-dichloropyrazine was coupled with piperazine-1-carboxylic acid tert-Bu ester using Na2CO3 in t-BuOH to give 6'-chloro-2,3,5,6-tetrahydro-[1,2']bipyrazinyl-4-carboxylic acid tert-Bu ester. Substitution with 3-chlorobenzyl alc. in the presence of KOH and 18-crown-6 in toluene followed by deesterification afforded 6'-(3-chlorobenzyloxy)-3,4,5,6-tetrahydro-2H-[1,2']bipyrazinyl (II). Compds. of the invention demonstrated affinity at the serotonin 5HT2A and 5HT2C binding sites with Ki values ranging from 0.5 nM to 1.0 μM and 0.1 nM to 586.5 nM, resp. In a functional assay using 5-HT2C expressed NIH 3T3 cells, II displayed EC50 ≤ 1.0 μM. I and pharmaceutical compns. containing I are useful for the treatment of diseases linked to the activation of 5-HT2 receptors, such as sexual dysfunction (no data).

IT 479685-11-5P, 5'-tert-Butoxycarbonylamino-6'-(3-chlorobenzyloxy)-2,3,5,6-tetrahydro-[1,2']bipyrazinyl-4-carboxylic acid tert-butyl ester
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of [1,2']bipyrazinyl 5-HT2 receptor ligands for treatment of sexual dysfunction and other 5-HT2 mediated disorders)

RN 479685-11-5 CAPLUS

CN 1-Piperazinecarboxylic acid, 4-[6-[(3-chlorophenyl)methoxy]-5-[[(1,1-dimethylethoxy)carbonyl]amino]pyrazinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 22 OF 41 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:107335 CAPLUS
DOCUMENT NUMBER: 136:151189
TITLE: Preparation of pyrazinyl-, pyridazinyl-, pyrimidinyl-, and pyridinyl-hexahydrodiazepines and their use as factor Xa inhibitors
INVENTOR(S): Herron, David Kent; Joseph, Sajan; Marquart, Angela Lynn; Masters, John Joseph; Mendel, David; Smith, Gerald Floyd; Waid, Philip Parker; Wiley, Michael Robert; Yee, Ying Kwong
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 159 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002010154	A2	20020207	WO 2001-US16528	20010718
WO 2002010154	A3	20020627		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001080438	A	20020213	AU 2001-80438	20010718
EP 1307444	A2	20030507	EP 2001-958825	20010718
EP 1307444	B1	20071003		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
AT 374765	T	20071015	AT 2001-958825	20010718
ES 2292607	T3	20080316	ES 2001-958825	20010718
US 20040097491	A1	20040520	US 2003-332120	20030102

US 7160878 B2 20070109
PRIORITY APPLN. INFO.: US 2000-221092P P 20000727
WO 2001-US16528 W 20010718
OTHER SOURCE(S): MARPAT 136:151189
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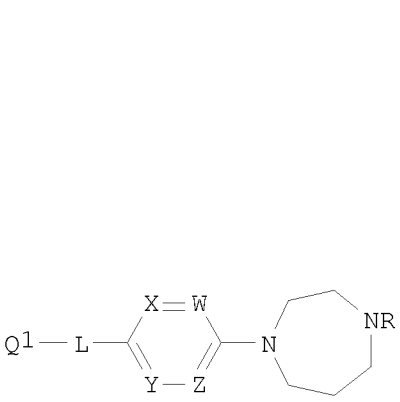

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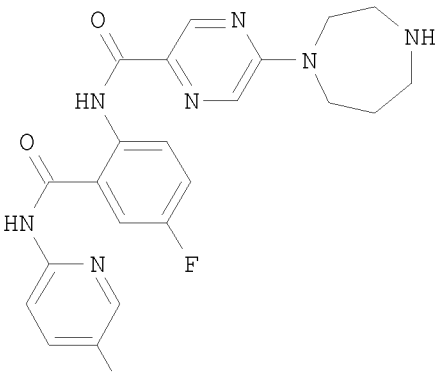


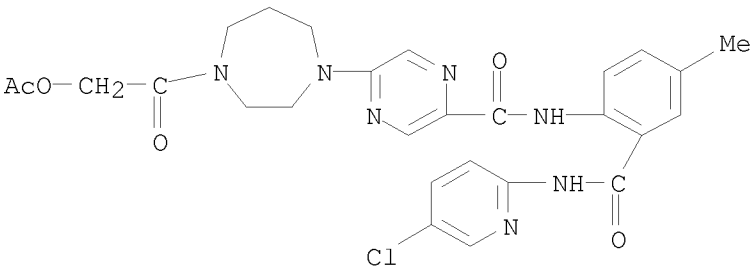
II

AB Substituted hexahydrodiazepines I [R = H, alkyl, acyl, acetyloxy, acetyl, aminoacetyl, alkylamido, etc.; one or two of X, W, Y, and Z equals N and each of the others of X, W, Y and Z is CH; when L = CO or CH2, Q1 = (un)substituted pyridinyl- or phenyl-amidophenylamine, in addition when L = CO, Q1 may equal Q2X2SO2N(CH2CH2)2N- wherein Q2 = (un)substituted Ph, benzo[b]thiophen-2-yl or naphthalen-2-yl (X2 = direct bond, CH2, ethylene, or ethen-1,2-diyl)], and their pharmaceutically acceptable salts are prepared and disclosed as factor Xa inhibitors. Thus, II was prepared by amidation of 2-amino-5-fluoro-N-(5-chloropyridin-2-yl)benzamide with 5-hydroxy-pyrazine-2-carboxylic acid (via its acid chloride) followed by substitution with 1-BOC-hexahydro-1,4-diazepine and subsequent deprotection of the diazepinyl nitrogen. As factor Xa inhibitors, the compds. of the invention are claimed to be useful in the treatment of thromboembolic disorders (no data).

IT 395684-26-1P 395684-27-2P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of pyrazinyl-, pyridazinyl-, pyrimidinyl-, and pyridinyl-hexahydrodiazepines as factor Xa inhibitors)

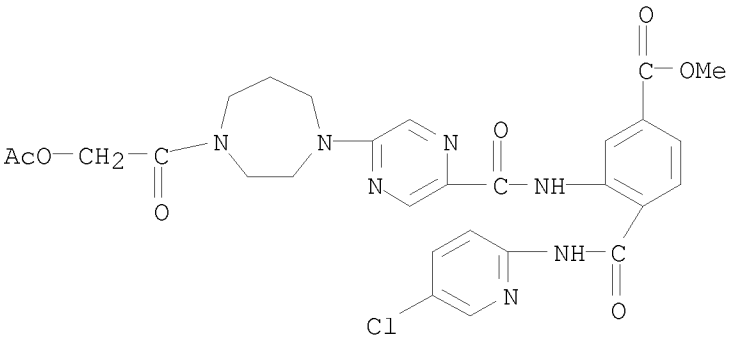
RN 395684-26-1 CAPLUS

CN Pyrazinecarboxamide, 5-[4-[(acetyloxy)acetyl]hexahydro-1H-1,4-diazepin-1-yl]-N-[2-[[(5-chloro-2-pyridinyl)amino]carbonyl]-4-methylphenyl]- (9CI) (CA INDEX NAME)



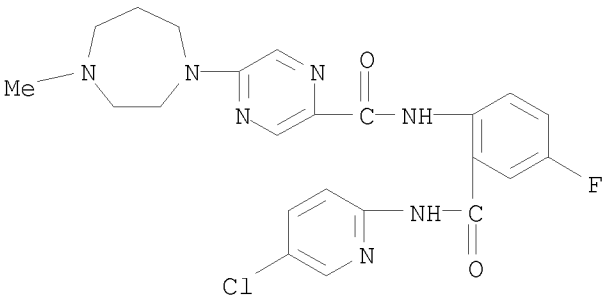
RN 395684-27-2 CAPLUS

CN Benzoic acid, 3-[[[5-[4-[(acetyloxy)acetyl]hexahydro-1H-1,4-diazepin-1-yl]pyrazinyl]carbonyl]amino]-4-[[(5-chloro-2-pyridinyl)amino]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

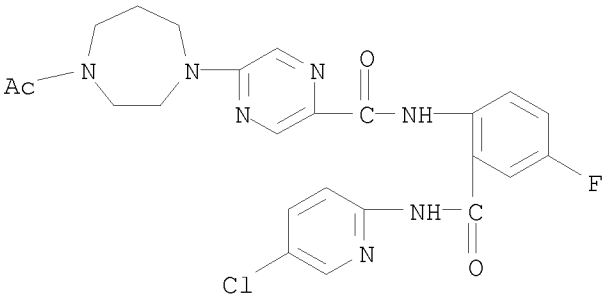


IT 395683-85-9P 395683-86-0P 395683-87-1P
395683-88-2P 395683-89-3P 395683-90-6P
395683-91-7P 395683-92-8P 395683-93-9P
395683-94-0P 395683-95-1P 395683-96-2P
395683-97-3P 395684-28-3P 395684-29-4P
395684-30-7P 395684-31-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrazinyl-, pyridazinyl-, pyrimidinyl-, and pyridinyl-hexahydrodiazepines as factor Xa inhibitors)

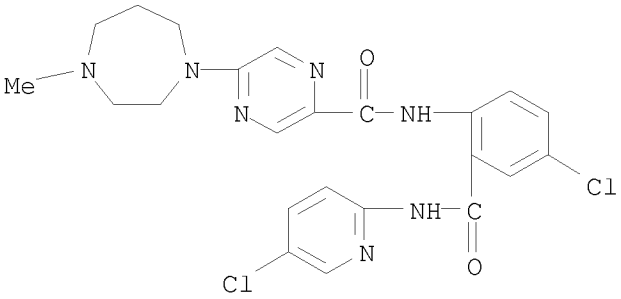
RN 395683-85-9 CAPLUS
CN Pyrazinecarboxamide, N-[2-[[(5-chloro-2-pyridinyl)amino]carbonyl]-4-fluorophenyl]-5-(hexahydro-4-methyl-1H-1,4-diazepin-1-yl)- (9CI) (CA INDEX NAME)



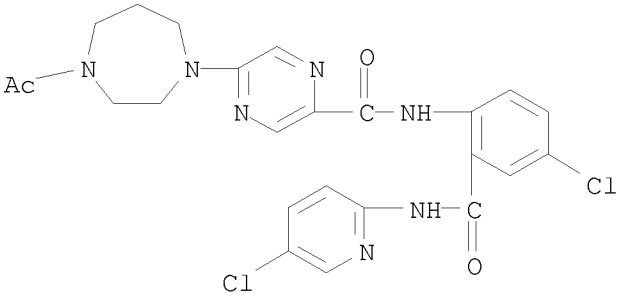
RN 395683-86-0 CAPLUS
CN Pyrazinecarboxamide, 5-(4-acetylhexahydro-1H-1,4-diazepin-1-yl)-N-[2-[[(5-chloro-2-pyridinyl)amino]carbonyl]-4-fluorophenyl]- (9CI) (CA INDEX NAME)



RN 395683-87-1 CAPLUS
CN Pyrazinecarboxamide, N-[4-chloro-2-[[(5-chloro-2-pyridinyl)amino]carbonyl]phenyl]-5-(hexahydro-4-methyl-1H-1,4-diazepin-1-yl)- (9CI) (CA INDEX NAME)



RN 395683-88-2 CAPLUS
CN Pyrazinecarboxamide, 5-(4-acetylhexahydro-1H-1,4-diazepin-1-yl)-N-[4-chloro-2-[[(5-chloro-2-pyridinyl)amino]carbonyl]phenyl]- (9CI) (CA INDEX NAME)



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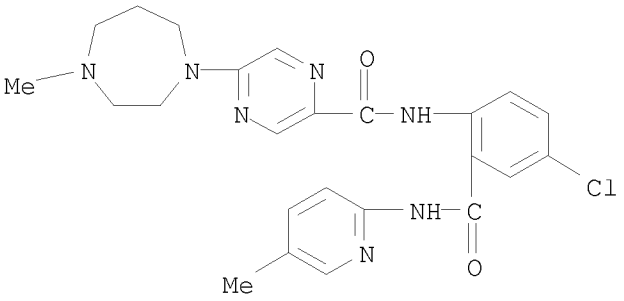
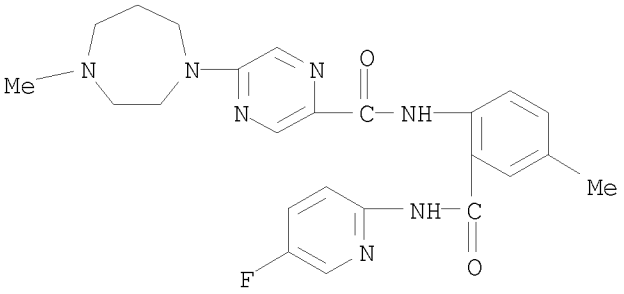
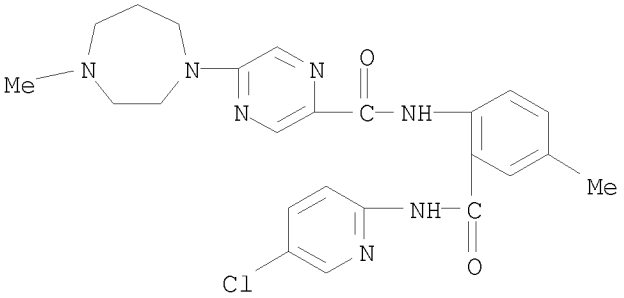
CN Pyrazinecarboxamide, N-[4-chloro-2-[[(5-methyl-2-pyridinyl)amino]carbonyl]phenyl]-5-(hexahydro-4-methyl-1H-1,4-diazepin-1-yl)- (9CI) (CA INDEX NAME)



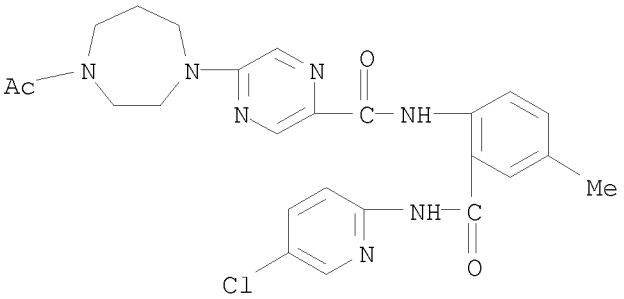
RN 395683-90-6 CAPLUS
CN Pyrazinecarboxamide, N-[2-[[(5-fluoro-2-pyridinyl)amino]carbonyl]-4-methylphenyl]-5-(hexahydro-4-methyl-1H-1,4-diazepin-1-yl)- (9CI) (CA INDEX NAME)



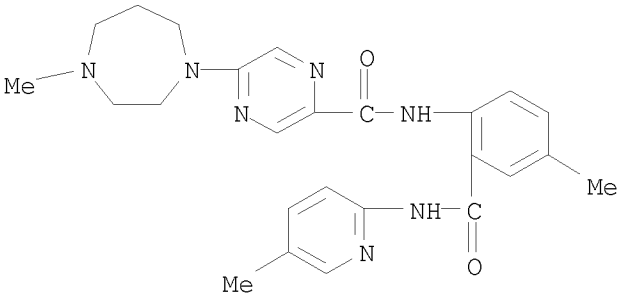
RN 395683-91-7 CAPLUS
CN Pyrazinecarboxamide, N-[2-[[(5-chloro-2-pyridinyl)amino]carbonyl]-4-methylphenyl]-5-(hexahydro-4-methyl-1H-1,4-diazepin-1-yl)- (9CI) (CA INDEX NAME)



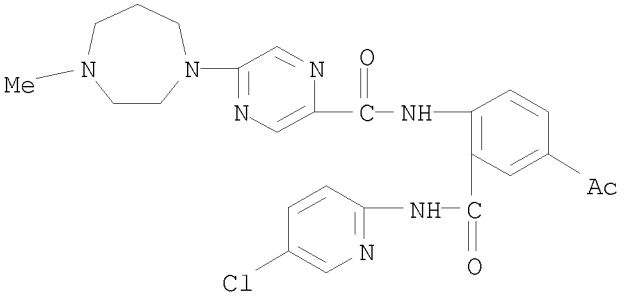
RN 395683-92-8 CAPLUS
CN Pyrazinecarboxamide, 5-(4-acetylhexahydro-1H-1,4-diazepin-1-yl)-N-[2-[[(5-chloro-2-pyridinyl)amino]carbonyl]-4-methylphenyl]- (9CI) (CA INDEX NAME)



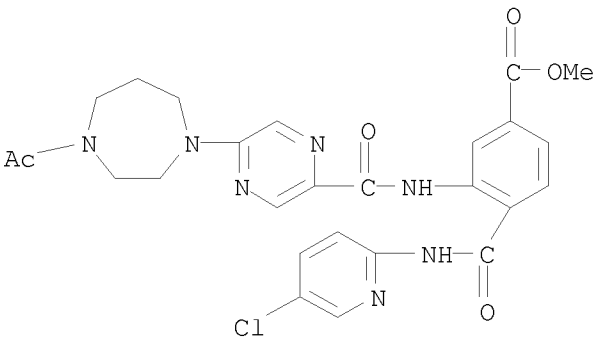
RN 395683-93-9 CAPLUS
CN Pyrazinecarboxamide, 5-(hexahydro-4-methyl-1H-1,4-diazepin-1-yl)-N-[4-methyl-2-[[(5-methyl-2-pyridinyl)amino]carbonyl]phenyl]- (9CI) (CA INDEX NAME)



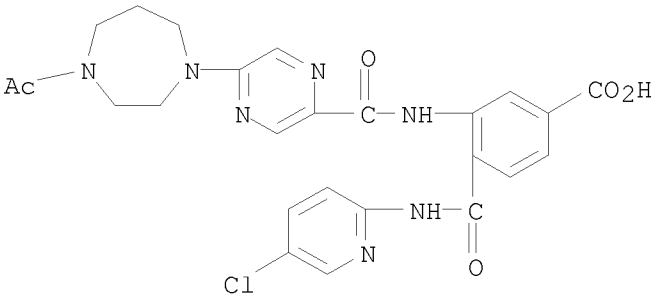
RN 395683-94-0 CAPLUS
CN Pyrazinecarboxamide, N-[4-acetyl-2-[[(5-chloro-2-pyridinyl)amino]carbonyl]phenyl]-5-(hexahydro-4-methyl-1H-1,4-diazepin-1-yl)- (9CI) (CA INDEX NAME)



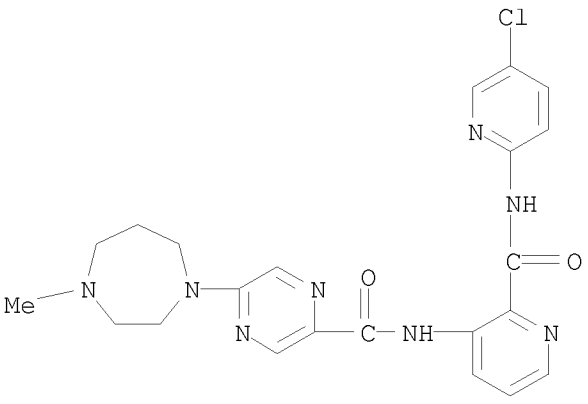
RN 395683-95-1 CAPLUS
CN Benzoic acid, 3-[[[5-(4-acetylhexahydro-1H-1,4-diazepin-1-yl)pyrazinyl]carbonyl]amino]-4-[[(5-chloro-2-pyridinyl)amino]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



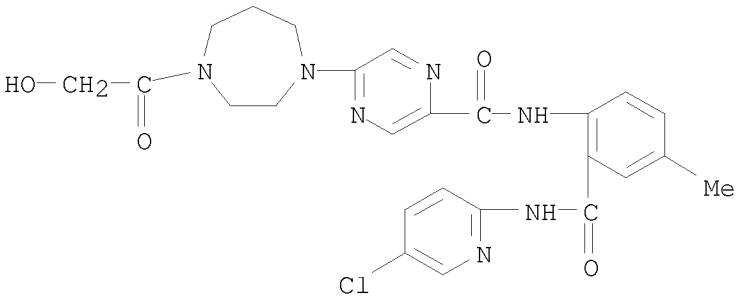
RN 395683-96-2 CAPLUS
CN Benzoic acid, 3-[[[5-(4-acetylhexahydro-1H-1,4-diazepin-1-yl)pyrazinyl]carbonyl]amino]-4-[[(5-chloro-2-pyridinyl)amino]carbonyl]- (9CI) (CA INDEX NAME)



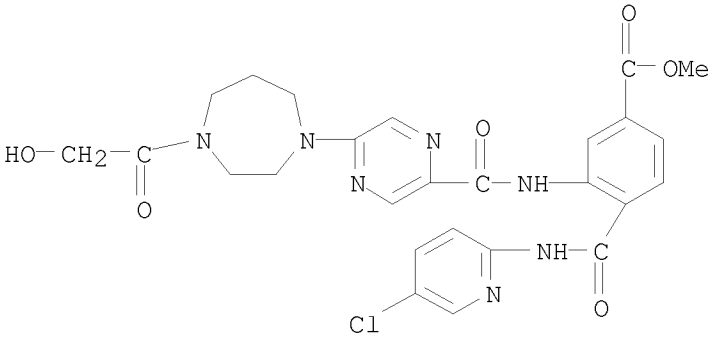
RN 395683-97-3 CAPLUS
CN Pyrazinecarboxamide, N-[2-[[(5-chloro-2-pyridinyl)amino]carbonyl]-3-pyridinyl]-5-(hexahydro-4-methyl-1H-1,4-diazepin-1-yl)- (9CI) (CA INDEX NAME)



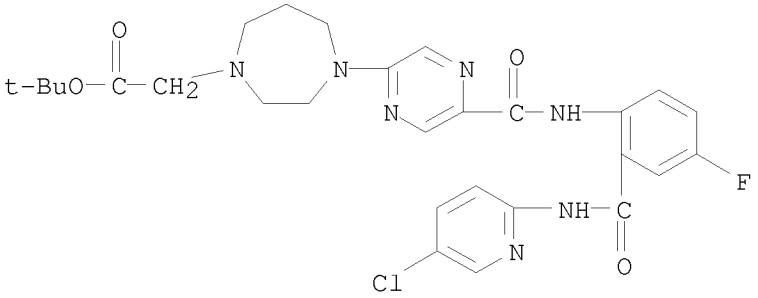
RN 395684-28-3 CAPLUS
CN Pyrazinecarboxamide, N-[2-[[(5-chloro-2-pyridinyl)amino]carbonyl]-4-methylphenyl]-5-[hexahydro-4-(hydroxyacetyl)-1H-1,4-diazepin-1-yl]- (9CI) (CA INDEX NAME)



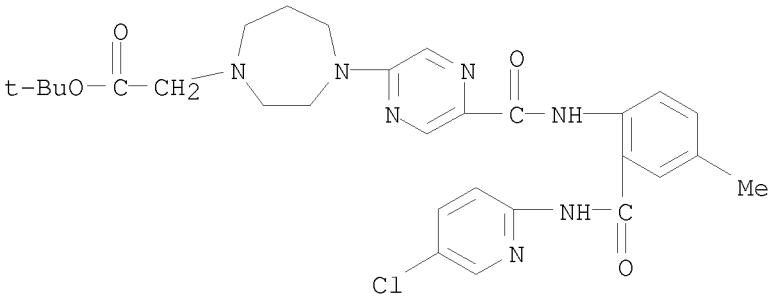
RN 395684-29-4 CAPLUS
CN Benzoic acid, 4-[[(5-chloro-2-pyridinyl)amino]carbonyl]-3-[[[5-[hexahydro-4-(hydroxyacetyl)-1H-1,4-diazepin-1-yl]pyrazinyl]carbonyl]amino]-, methyl ester (9CI) (CA INDEX NAME)



RN 395684-30-7 CAPLUS
CN 1H-1,4-Diazepine-1-acetic acid, 4-[5-[[[2-[[(5-chloro-2-pyridinyl)amino]carbonyl]-4-fluorophenyl]amino]carbonyl]pyrazinyl]hexahydro-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

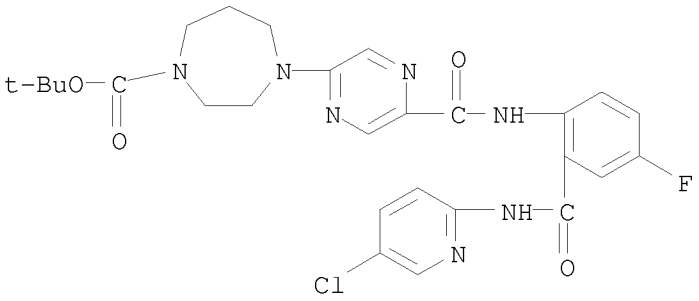


RN 395684-31-8 CAPLUS
CN 1H-1,4-Diazepine-1-acetic acid, 4-[5-[[[2-[[(5-chloro-2-pyridinyl)amino]carbonyl]-4-methylphenyl]amino]carbonyl]pyrazinyl]hexahydro-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

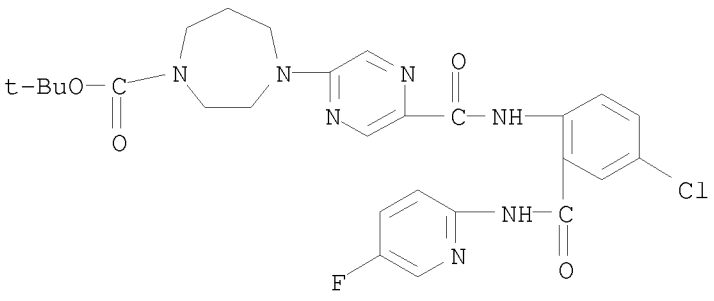


IT 395684-83-0P 395684-84-1P 395684-85-2P
395684-86-3P 395684-87-4P 395684-88-5P
395684-89-6P 395684-90-9P 395684-91-0P
395684-92-1P 395684-93-2P 395684-94-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of pyrazinyl-, pyridazinyl-, pyrimidinyl-, and pyridinyl-hexahydrodiazepines as factor Xa inhibitors)

RN 395684-83-0 CAPLUS
CN 1H-1,4-Diazepine-1-carboxylic acid, 4-[5-[[[2-[[(5-chloro-2-pyridinyl)amino]carbonyl]-4-fluorophenyl]amino]carbonyl]pyrazinyl]hexahydro-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

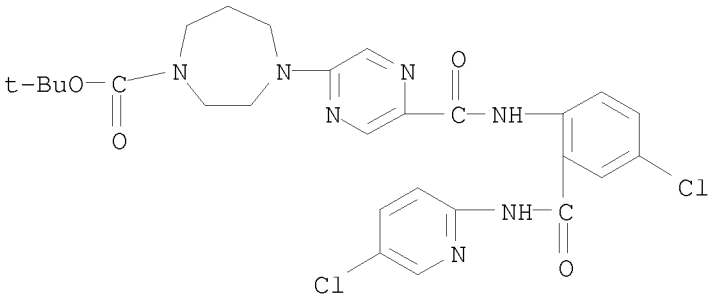


RN 395684-84-1 CAPLUS
CN 1H-1,4-Diazepine-1-carboxylic acid, 4-[5-[[[4-chloro-2-[[(5-fluoro-2-pyridinyl)amino]carbonyl]phenyl]amino]carbonyl]pyrazinyl]hexahydro-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

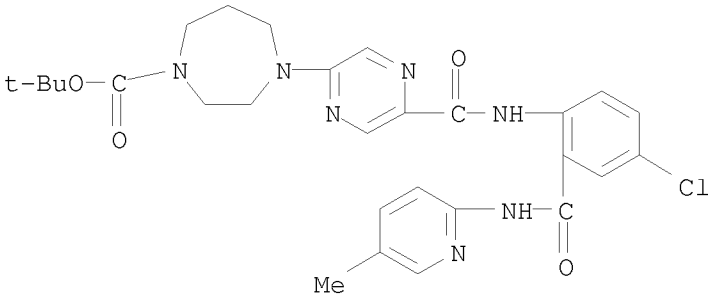


RN 395684-85-2 CAPLUS
CN 1H-1,4-Diazepine-1-carboxylic acid, 4-[5-[[[4-chloro-2-[[(5-chloro-2-pyridinyl)amino]carbonyl]phenyl]amino]carbonyl]pyrazinyl]hexahydro-,

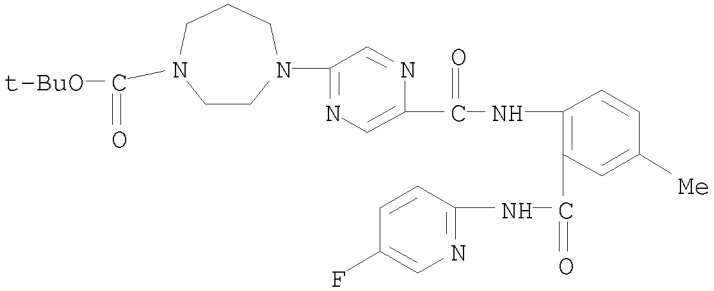
1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



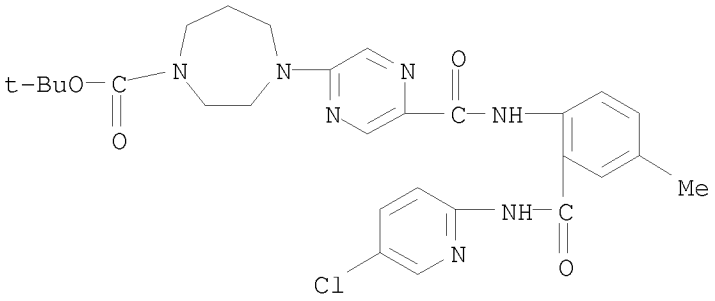
RN 395684-86-3 CAPLUS
CN 1H-1,4-Diazepine-1-carboxylic acid, 4-[5-[[[4-chloro-2-[[(5-methyl-2-pyridinyl)amino]carbonyl]phenyl]amino]carbonyl]pyrazinyl]hexahydro-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



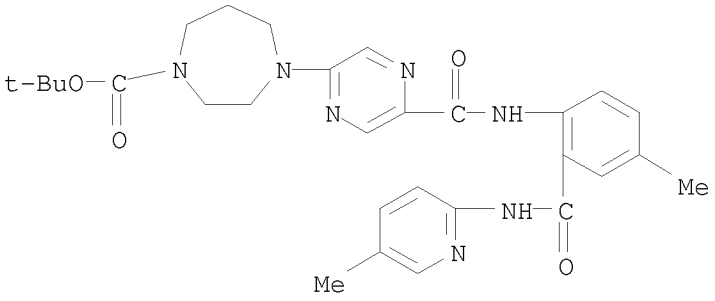
RN 395684-87-4 CAPLUS
CN 1H-1,4-Diazepine-1-carboxylic acid, 4-[5-[[[2-[[(5-fluoro-2-pyridinyl)amino]carbonyl]-4-methylphenyl]amino]carbonyl]pyrazinyl]hexahydro-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



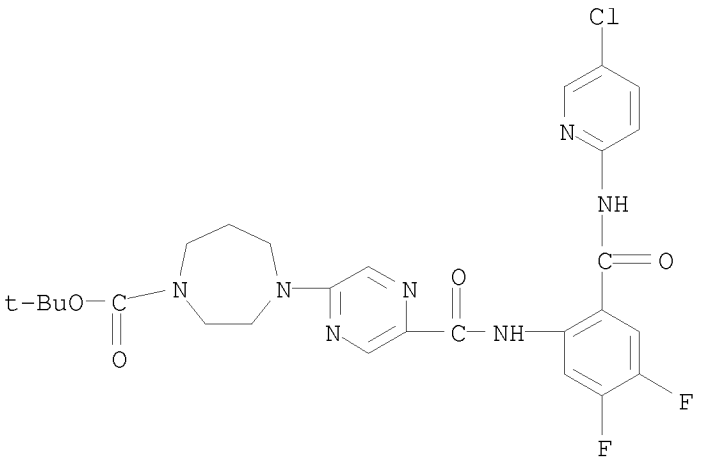
RN 395684-88-5 CAPLUS
CN 1H-1,4-Diazepine-1-carboxylic acid, 4-[5-[[[2-[[(5-chloro-2-pyridinyl)amino]carbonyl]-4-methylphenyl]amino]carbonyl]pyrazinyl]hexahydro-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



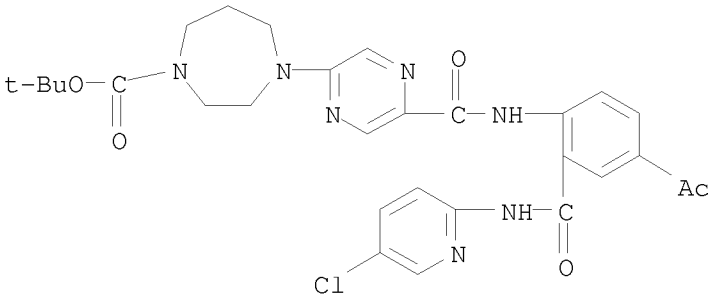
RN 395684-89-6 CAPLUS
CN 1H-1,4-Diazepine-1-carboxylic acid, hexahydro-4-[5-[[[4-methyl-2-[[(5-methyl-2-pyridinyl)amino]carbonyl]phenyl]amino]carbonyl]pyrazinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



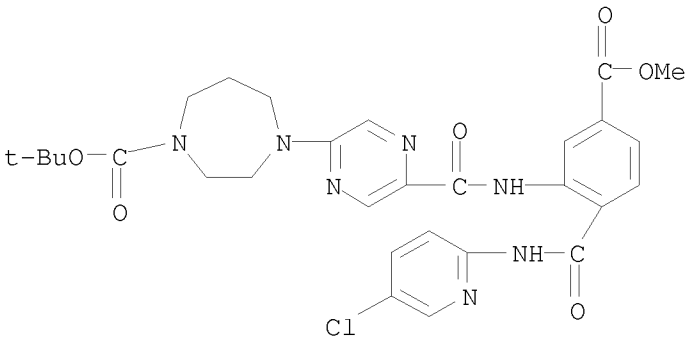
RN 395684-90-9 CAPLUS
CN 1H-1,4-Diazepine-1-carboxylic acid, 4-[5-[[[2-[[(5-chloro-2-pyridinyl)amino]carbonyl]-4,5-difluorophenyl]amino]carbonyl]pyrazinyl]hexahydro-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



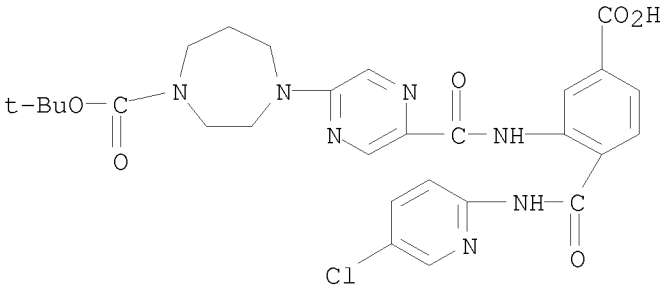
RN 395684-91-0 CAPLUS
CN 1H-1,4-Diazepine-1-carboxylic acid, 4-[5-[[[4-acetyl-2-[[(5-chloro-2-pyridinyl)amino]carbonyl]phenyl]amino]carbonyl]pyrazinyl]hexahydro-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



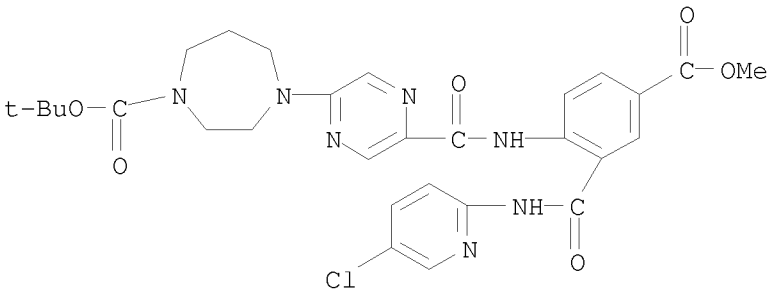
RN 395684-92-1 CAPLUS
CN 1H-1,4-Diazepine-1-carboxylic acid, 4-[5-[[[2-[[(5-chloro-2-pyridinyl)amino]carbonyl]-5-(methoxycarbonyl)phenyl]amino]carbonyl]pyrazinyl]hexahydro-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 395684-93-2 CAPLUS
CN 1H-1,4-Diazepine-1-carboxylic acid, 4-[5-[[[5-carboxy-2-[[(5-chloro-2-pyridinyl)amino]carbonyl]phenyl]amino]carbonyl]pyrazinyl]hexahydro-, 1-(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



RN 395684-94-3 CAPLUS
CN 1H-1,4-Diazepine-1-carboxylic acid, 4-[5-[[[2-[[(5-chloro-2-pyridinyl)amino]carbonyl]-4-(methoxycarbonyl)phenyl]amino]carbonyl]pyrazinyl]hexahydro-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 23 OF 41 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1995:328907 CAPLUS
DOCUMENT NUMBER: 123:199334
ORIGINAL REFERENCE NO.: 123:35613a,35616a
TITLE: Synthesis, antiviral activity, and bioavailability studies of γ-lactam derived HIV protease inhibitors
AUTHOR(S): Hungate, Randall W.; Chen, Jenny L.; Starbuck, Ken E.; Vacca, Joseph P.; McDaniel, Stacey L.; Levin, Rhonda B.; Dorsey, Bruce D.; Guare, James P.; Holloway, M. Katharine; et al.
CORPORATE SOURCE: Merck Research Laboratories, West Point, PA, 19486, USA
SOURCE: Bioorganic & Medicinal Chemistry (1994), 2(9), 859-79
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

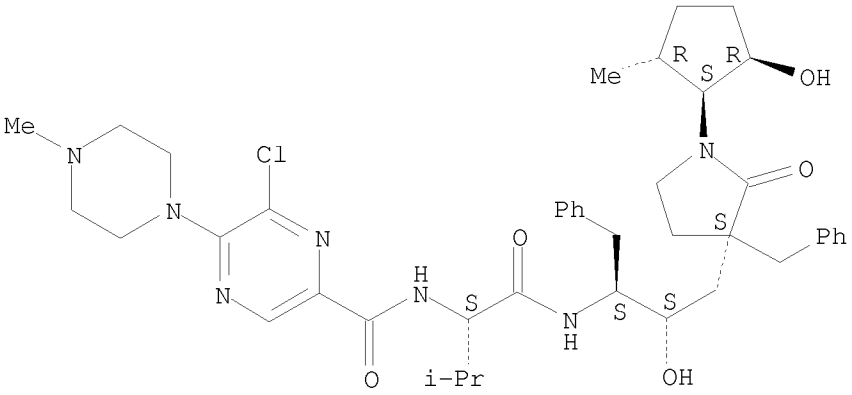
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Incorporation of a γ-lactam in hydroxyethylene isosteres results in modest inhibitors of HIV-1 protease. Addnl. structural activity studies have produced significantly more potent inhibitors with the introduction of the trisubstituted cyclopentane (e.g., pyrrolidinone I) as the optimum substituent for the C-terminus. This new amino acid amide surrogate can be readily prepared in large scale from (R)-pulegone. Optimized compds. (valinylamino) pyrrolidinones II and III are potent antiviral agents and are well absorbed (15-20%) in a dog model after oral administration.

IT 167640-94-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation, antiviral, and HIV-1 protease inhibitory activity of γ-lactams)

RN 167640-94-0 CAPLUS
CN Pyrazinecarboxamide, 6-chloro-N-[1-[[[2-hydroxy-3-[1-(2-hydroxy-5-methylcyclopentyl)-2-oxo-3-(phenylmethyl)-3-pyrrolidinyl]-1-(phenylmethyl)propyl]amino]carbonyl]-2-methylpropyl]-5-(4-methyl-1-piperazinyl)-, [1S-[1α[R*[1R*(R*),2R*]],2α,5β]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L5 ANSWER 24 OF 41 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1993:603375 CAPLUS
DOCUMENT NUMBER: 119:203375
ORIGINAL REFERENCE NO.: 119:36273a,36276a
TITLE: Potent HIV protease inhibitors: the development of tetrahydrofuranylglycines as novel P2-ligands and pyrazine amides as P3-ligands
AUTHOR(S): Ghosh, Arun K.; Thompson, Wayne J.; Holloway, M. Katharine; McKee, Sean P.; Duong, Tien T.; Lee, Hee Yoon; Munson, Peter M.; Smith, Anthony M.; Wai, Jenny M.; et al.
CORPORATE SOURCE: Dep. Med. Chem., Merck Res. Lab., West Point, PA, 19486, USA
SOURCE: Journal of Medicinal Chemistry (1993), 36(16), 2300-10
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 119:203375
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

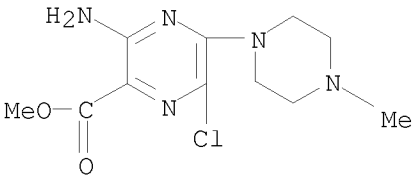
AB A series of protease inhibitors bearing constrained unnatural amino acids at the P2-position and novel heterocycles at the P3-position of compound I (R = R1; Ro 31-8959) were synthesized, and their in vitro enzyme inhibitory and antiviral activities were evaluated. Replacement of P2-asparagine of compound I (R = R1) with (2S,3'R)-tetrahydrofuranylglycine resulted in improvement in enzyme inhibitory as well as antiviral potencies (compound I; R = R2). Interestingly, incorporation of (2S,3'S)-tetrahydrofuranylglycine at the P2-position proved to be less effective. The resulting compound I (R = R3) was 100-fold less potent than the 2S,3R-isomer (compound I; R = R2). This stereochem. preference indicated a hydrogen-bonding interaction between the tetrahydrofuranyl oxygen and the residues of the S2-region of the enzyme active site. Furthermore, replacement of P3-quinolinoyl ligand of I (R = R1) with various novel heterocycles resulted in potent inhibitors of HIV proteases. Of particular interest, compound I (R = R4) with (2S,3'R)-tetrahydrofuranylglycine at P2 and pyrazine derivative at P3 is one of the most potent inhibitors of HIV-1 (IC50 value 0.07 nM) and HIV-2 (IC50 value 0.18 nM) proteases. Another important result in this series is the identification of compound I (R = R5) in which the P2-P3-amide carbonyl has been removed. The resulting compound I (R = R5) has exhibited improvement

in antiviral potency while retaining the enzyme inhibitory potency similar to compound I (R = R1).

IT 1151-35-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(bromination of)

RN 1151-35-5 CAPLUS

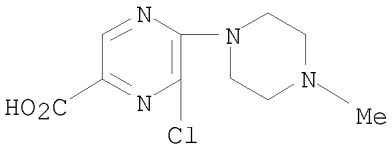
CN Pyrazinecarboxylic acid, 3-amino-6-chloro-5-(4-methyl-1-piperazinyl)-, methyl ester (7CI, 8CI, 9CI) (CA INDEX NAME)



IT 150318-48-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and amidation of, by [aminohydroxyphenylbutyl)perhydroisoquinolinecarboxamide derivative)

RN 150318-48-2 CAPLUS

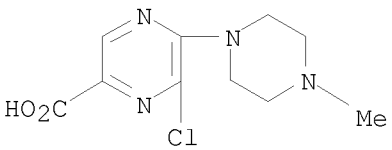
CN Pyrazinecarboxylic acid, 6-chloro-5-(4-methyl-1-piperazinyl)-, monohydrochloride (9CI) (CA INDEX NAME)



IT 150331-98-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and saponification of)

RN 150331-98-9 CAPLUS

CN Pyrazinecarboxylic acid, 6-chloro-5-(4-methyl-1-piperazinyl)- (9CI) (CA INDEX NAME)

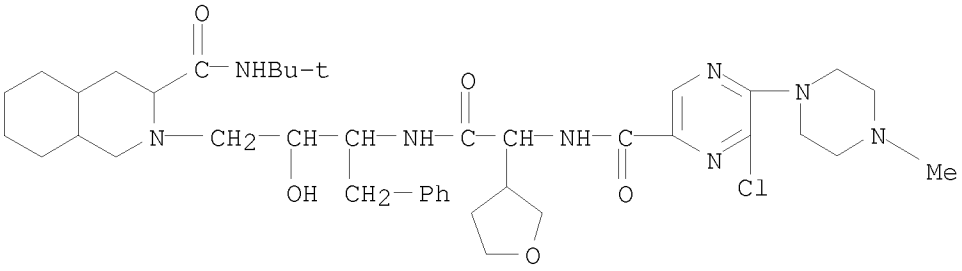


IT 150331-78-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation, HIV-1 protease inhibition and antiviral activity of)

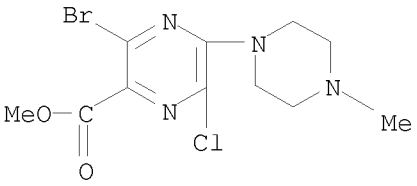
RN 150331-78-5 CAPLUS

CN 3-Isoquinolinecarboxamide, 2-[3-[[[[[6-chloro-5-(4-methyl-1-

piperazinyl)pyrazinyl]carbonyl]amino](tetrahydro-3-furanyl)acetyl]amino]-2-hydroxy-4-phenylbutyl]-N-(1,1-dimethylethyl)decahydro-, [3S-[2[2S*,3R*[R*(S*)]],3α,4aβ,8aβ]]- (9CI) (CA INDEX NAME)



IT 150331-79-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation, hydrogenolysis, and saponification of)
RN 150331-79-6 CAPLUS
CN Pyrazinecarboxylic acid, 3-bromo-6-chloro-5-(4-methyl-1-piperazinyl)-, methyl ester (9CI) (CA INDEX NAME)



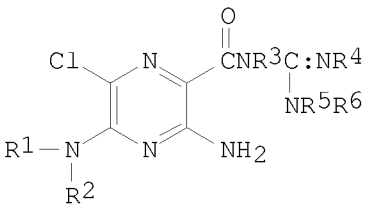
L5 ANSWER 25 OF 41 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1993:449413 CAPLUS
DOCUMENT NUMBER: 119:49413
ORIGINAL REFERENCE NO.: 119:8969a,8972a
TITLE: New pyrazine derivatives, their preparation and their use as ingredients in drugs
INVENTOR(S): Koeppe, Herbert; Speck, Georg; Stockhaus, Klaus
PATENT ASSIGNEE(S): Boehringer Ingelheim International G.m.b.H., Germany; Boehringer Ingelheim KG
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9304048	A1	19930304	WO 1992-EP1738	19920731
W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
DE 4127026	A1	19930218	DE 1991-4127026	19910816
DE 4130461	A1	19930318	DE 1991-4130461	19910913

AU 9223870	A	19930316	AU 1992-23870		19920731
AU 669122	B2	19960530			
EP 598770	A1	19940601	EP 1992-916697		19920731
EP 598770	B1	19971015			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE					
JP 06509798	T	19941102	JP 1992-504057		19920731
NO 9400523	A	19940215	NO 1994-523		19940215
PRIORITY APPLN. INFO.:			DE 1991-4127026	A	19910816
			DE 1991-4130461	A	19910913
			WO 1992-EP1738	A	19920731

OTHER SOURCE(S): CASREACT 119:49413; MARPAT 119:49413

GI



I

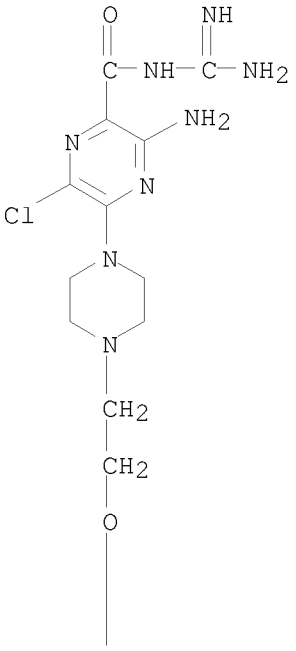
AB A process for the preparation of pyrazine derivative I where R1 = H or alkyl, R2 = functionalized alkyl moiety, R3, R5 = H and R4, R6 = H, Me, Et, Bu, benzyl was accomplished by conventional methods. E.g., reaction of 4.44 g of Me 3-amino-5,6-dichloropyrazine-2-carboxylate and 3.6 g of 2-amino-1-(2,6-dimethylphenoxy)propane with 2.2 g Et3N in 40 mL anhydrous DMF gave an intermediate pyrazinecarboxylic acid ester which underwent subsequent ammonolysis in 50 mL MeOH and 80mL of methanolic guanidine solution and eluted on silica gel by AcOH:i-PrOH:NH3 eluent to give N-amidino-3-amino-6-chloro-5-(2-[1-(2,6-dimethylphenoxy)]propylamino)pyrazine-2-carboxamide-hydrochloride. The products are suitable for use as active ingredients in drugs (no data).

IT 147894-04-0P 147932-14-7P 147932-15-8P
147932-16-9P 147932-17-0P 147932-18-1P
147932-20-5P 147932-21-6P 147932-22-7P
147932-23-8P 148296-52-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 147894-04-0 CAPLUS

CN Pyrazinecarboxamide, 3-amino-N-(aminoiminomethyl)-6-chloro-5-[4-[2-(3-methoxyphenoxy)ethyl]-1-piperazinyl]-, dihydrobromide (9CI) (CA INDEX NAME)

PAGE 1-A



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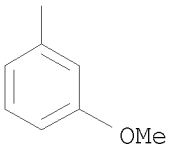
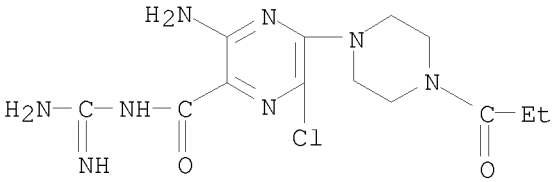


● 2 HBr

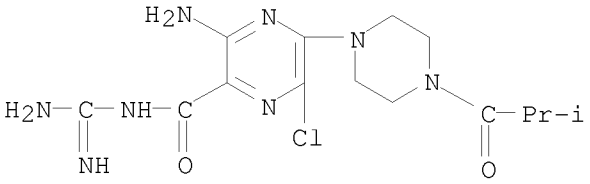
RN 147932-14-7 CAPLUS
CN Pyrazinecarboxamide, 3-amino-N-(aminoiminomethyl)-6-chloro-5-[4-(1-oxopropyl)-1-piperazinyl]-, monohydrochloride (9CI) (CA INDEX NAME)



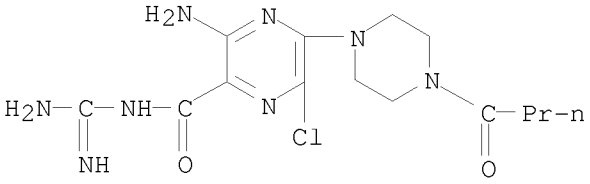
● HCl

RN 147932-15-8 CAPLUS
CN Pyrazinecarboxamide, 3-amino-N-(aminoiminomethyl)-6-chloro-5-[4-(2-methyl-

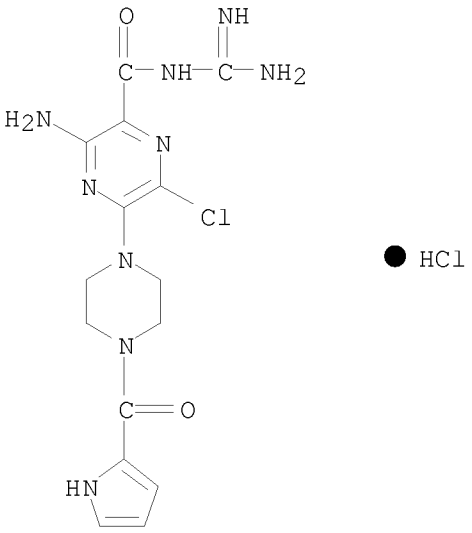
1-oxopropyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



RN 147932-16-9 CAPLUS
CN Pyrazinecarboxamide, 3-amino-N-(aminoiminomethyl)-6-chloro-5-[4-(1-oxobutyl)-1-piperazinyl]-, monohydrochloride (9CI) (CA INDEX NAME)



RN 147932-17-0 CAPLUS
CN Pyrazinecarboxamide, 3-amino-N-(aminoiminomethyl)-6-chloro-5-[4-(1H-pyrrol-2-ylcarbonyl)-1-piperazinyl]-, monohydrochloride (9CI) (CA INDEX NAME)



RN 147932-18-1 CAPLUS
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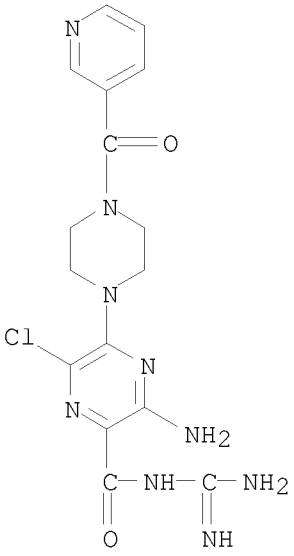
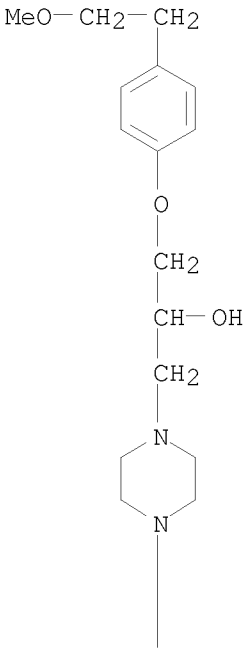


RN 147932-20-5 CAPLUS
CN Pyrazinecarboxamide, 3-amino-N-(aminoiminomethyl)-6-chloro-5-[4-[2-hydroxy-3-[4-(2-methoxyethyl)phenoxy]propyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



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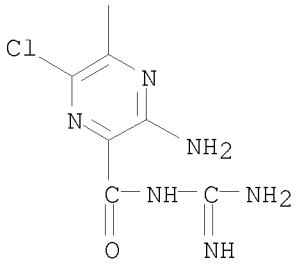
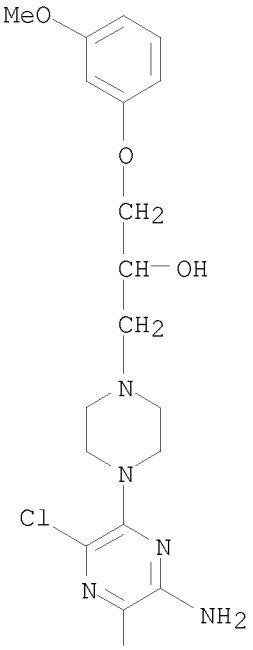


RN 147932-21-6 CAPLUS
CN Pyrazinecarboxamide, 3-amino-N-(aminoiminomethyl)-6-chloro-5-[4-[2-hydroxy-3-(3-methoxyphenoxy)propyl]-1-piperazinyl]-, dihydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A



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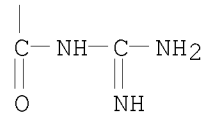
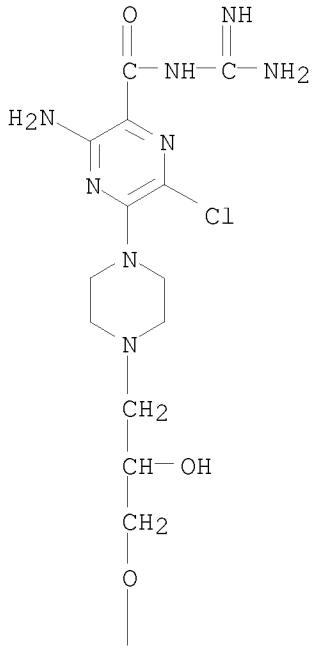


●2 HCl

RN 147932-22-7 CAPLUS
CN Pyrazinecarboxamide, 3-amino-N-(aminoiminomethyl)-6-chloro-5-[4-[2-hydroxy-3-(1-naphthalenyloxy)propyl]-1-piperazinyl]-, dihydrochloride (9CI) (CA

INDEX NAME)

PAGE 1-A



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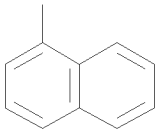

● 2 HCl

RN 147932-23-8 CAPLUS
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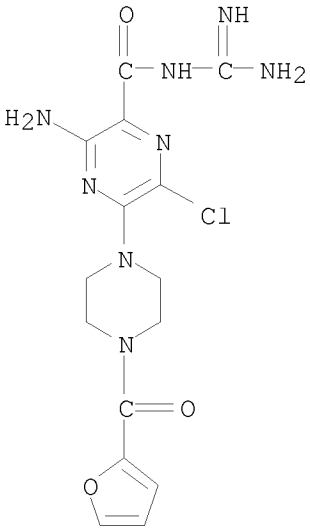

RN 148296-52-0 CAPLUS
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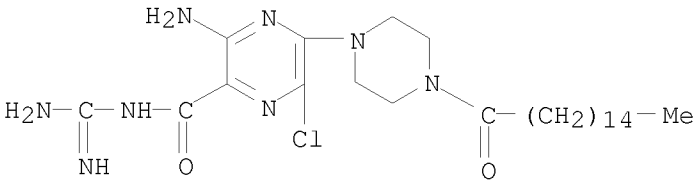

●2 HCl

L5 ANSWER 26 OF 41 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1993:408831 CAPLUS
DOCUMENT NUMBER: 119:8831
ORIGINAL REFERENCE NO.: 119:1817a,1820a
TITLE: Preparation of 2-guanidinocarbonyl-3,5-diamino-6-chloropyrazines as drugs
INVENTOR(S): Koeppe, Herbert; Speck, Georg; Stockhaus, Klaus
PATENT ASSIGNEE(S): Boehringer Ingelheim KG, Germany
SOURCE: Ger. Offen., 19 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4127026	A1	19930218	DE 1991-4127026	19910816
WO 9304048	A1	19930304	WO 1992-EP1738	19920731

W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE, US

RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG

AU 9223870	A	19930316	AU 1992-23870		19920731
AU 669122	B2	19960530			
EP 598770	A1	19940601	EP 1992-916697		19920731
EP 598770	B1	19971015			

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE

JP 06509798	T	19941102	JP 1992-504057		19920731
HU 67661	A2	19950428	HU 1994-430		19920731
CZ 280760	B6	19960417	CZ 1994-337		19920731
AT 159250	T	19971115	AT 1992-916697		19920731
ES 2108129	T3	19971216	ES 1992-916697		19920731
RU 2124008	C1	19981227	RU 1994-15265		19920731
ZA 9206132	A	19930331	ZA 1992-6132		19920814
NO 9400523	A	19940215	NO 1994-523		19940215
PRIORITY APPLN. INFO.:			DE 1991-4127026	A	19910816
			DE 1991-4130461	A	19910913
			WO 1992-EP1738	A	19920731

OTHER SOURCE(S): MARPAT 119:8831

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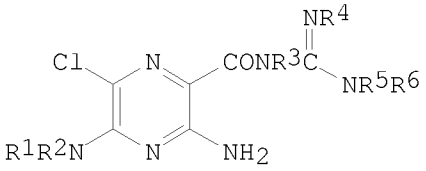
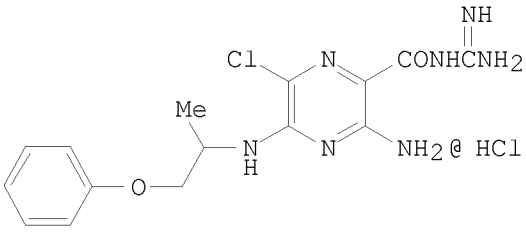


I



II

AB Title compds. [I; R1 = H, alkyl; R2 = morpholino, (substituted) alkyl, 4-piperidinyl, amidino; R1R2N = (substituted) piperidinyl, piperazinyl; R3-R6 = H, alkyl, PhCH2], effective inhibitors of Na+/H+ and Na+/Li+ exchange useful as antihypertensives, mucolytics, diuretics, neoplasm inhibitors, and platelet activating factor antagonists (no data), are prepared Thus, Me 3-amino-5,6-dichloropyrazine-2-carboxylate, 2-amino-1-(2,6-dimethylphenoxy)propane, and Et3N were heated in DMF at 95-100° for 1.5 h to give Me 3-amino-6-chloro-5-[2-[1-(2,6-dimethylphenoxy)]propylamino]pyrazine-2-carboxylate. This was heated with guanidine in MeOH to give title compound II.

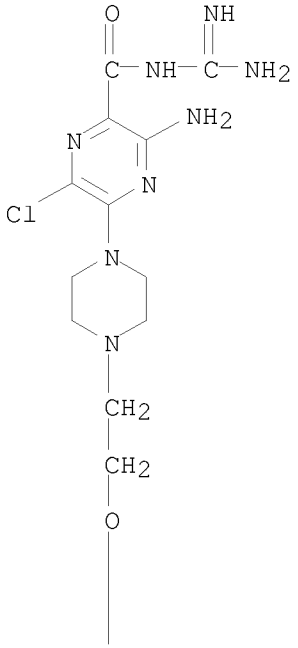
IT 147894-04-0P 147932-14-7P 147932-15-8P
147932-16-9P 147932-17-0P 147932-18-1P
147932-20-5P 147932-21-6P 147932-22-7P
147932-23-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as drug)

RN 147894-04-0 CAPLUS

CN Pyrazinecarboxamide, 3-amino-N-(aminoiminomethyl)-6-chloro-5-[4-[2-(3-

methoxyphenoxy)ethyl]-1-piperazinyl]-, dihydrobromide (9CI) (CA INDEX NAME)

PAGE 1-A



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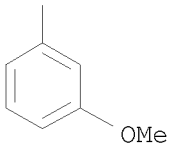
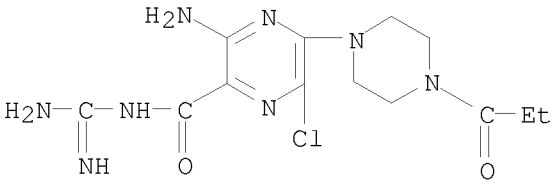


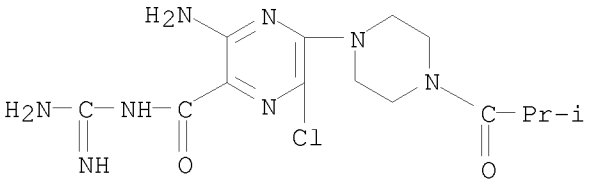
● 2 HBr

RN 147932-14-7 CAPLUS
CN Pyrazinecarboxamide, 3-amino-N-(aminoiminomethyl)-6-chloro-5-[4-(1-oxopropyl)-1-piperazinyl]-, monohydrochloride (9CI) (CA INDEX NAME)

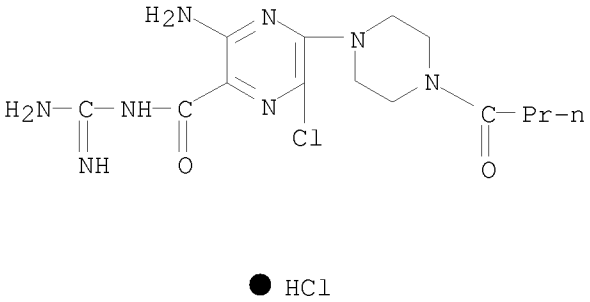


● HCl

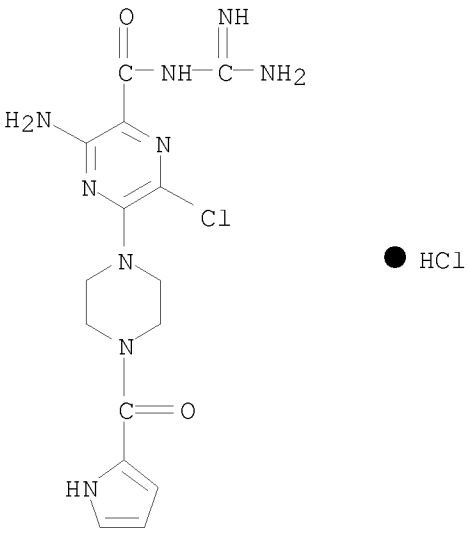
RN 147932-15-8 CAPLUS
CN Pyrazinecarboxamide, 3-amino-N-(aminoiminomethyl)-6-chloro-5-[4-(2-methyl-1-oxopropyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



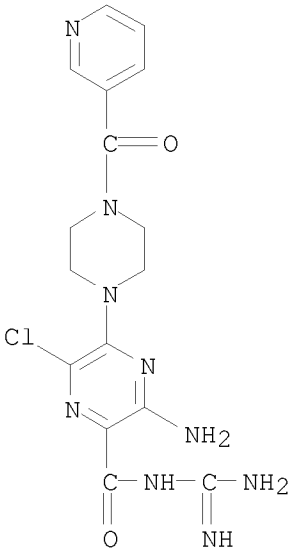
RN 147932-16-9 CAPLUS
CN Pyrazinecarboxamide, 3-amino-N-(aminoiminomethyl)-6-chloro-5-[4-(1-oxobutyl)-1-piperazinyl]-, monohydrochloride (9CI) (CA INDEX NAME)



RN 147932-17-0 CAPLUS
CN Pyrazinecarboxamide, 3-amino-N-(aminoiminomethyl)-6-chloro-5-[4-(1H-pyrrol-2-ylcarbonyl)-1-piperazinyl]-, monohydrochloride (9CI) (CA INDEX NAME)

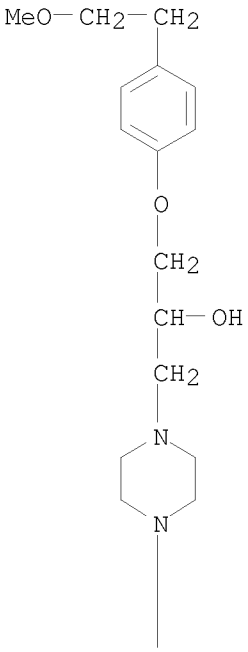


RN 147932-18-1 CAPLUS
CN Pyrazinecarboxamide, 3-amino-N-(aminoiminomethyl)-6-chloro-5-[4-(3-pyridinylcarbonyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



RN 147932-20-5 CAPLUS
CN Pyrazinecarboxamide, 3-amino-N-(aminoiminomethyl)-6-chloro-5-[4-[2-hydroxy-3-[4-(2-methoxyethyl)phenoxy]propyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



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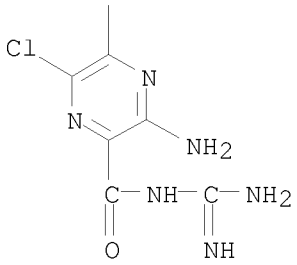
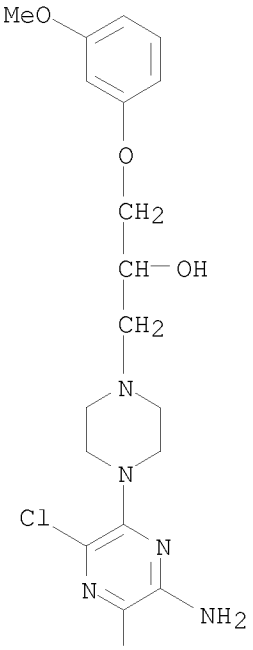


RN 147932-21-6 CAPLUS
CN Pyrazinecarboxamide, 3-amino-N-(aminoiminomethyl)-6-chloro-5-[4-[2-hydroxy-3-(3-methoxyphenoxy)propyl]-1-piperazinyl]-, dihydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A



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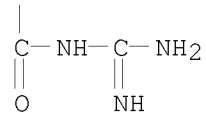

●2 HCl

RN 147932-22-7 CAPLUS
CN Pyrazinecarboxamide, 3-amino-N-(aminoiminomethyl)-6-chloro-5-[4-[2-hydroxy-3-(1-naphthalenyloxy)propyl]-1-piperazinyl]-, dihydrochloride (9CI) (CA

INDEX NAME)

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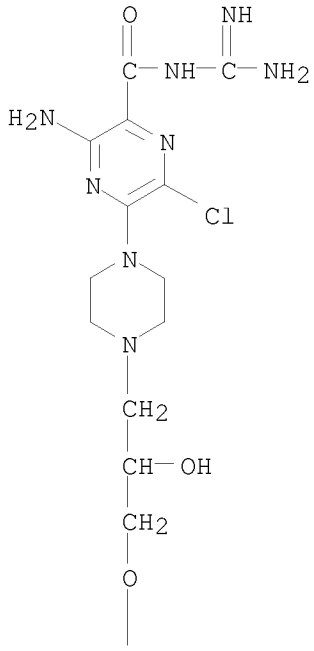

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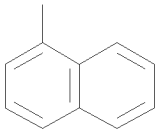

● 2 HCl

RN 147932-23-8 CAPLUS
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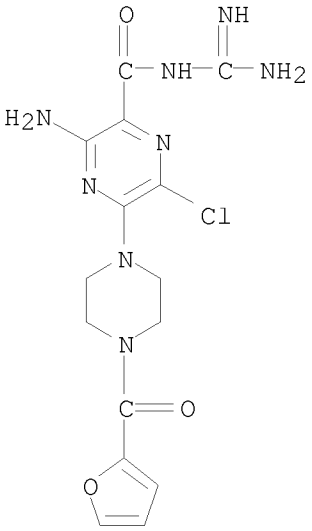
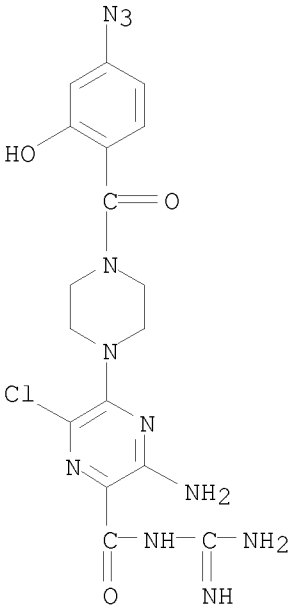


L5 ANSWER 27 OF 41 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1990:402710 CAPLUS
DOCUMENT NUMBER: 113:2710
ORIGINAL REFERENCE NO.: 113:551a,554a
TITLE: Photoactivatable probe for the sodium/hydrogen ion exchanger cross-links a 66-kDa renal brush border membrane protein
AUTHOR(S): Ross, Willie; Bertrand, William; Morrison, Aubrey
CORPORATE SOURCE: Sch. Med., Washington Univ., St. Louis, MO, 63110, USA
SOURCE: Journal of Biological Chemistry (1990), 265(10), 5341-4
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Earlier studies on LLC-PK1 cells have demonstrated 2 pharmacol. distinct Na+/H+ exchangers in renal epithelia. In addition, the cDNA clone for the human Na+/H+ antiporter which is growth factor activatable has been isolated and expressed (Sardet, C., et al., 1989). Here the synthesis of an amiloride analog that can be photoactivated and labeled with 125I is reported. This analog covalently crosslinks a 66-kDa protein of bovine renal brush border membranes. A rabbit polyclonal antibody that was directed against a 20-amino acid peptide of the cytoplasmic domain of its human Na+/H+ antiporter also gives a pos. Western against 66-kDa protein of bovine brush border membranes. Thus, the photoactive probe may be helpful in the isolation and purification of the brush border Na+/H+ exchanger.

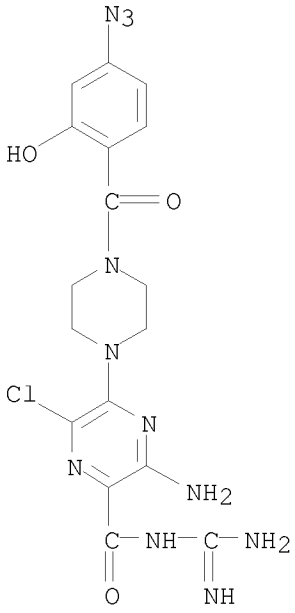
IT 127628-92-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and radioiodonation of)

RN 127628-92-6 CAPLUS
CN Pyrazinecarboxamide, 3-amino-N-(aminoiminomethyl)-5-[4-(4-azido-2-hydroxybenzoyl)-1-piperazinyl]-6-chloro- (9CI) (CA INDEX NAME)



IT 127513-40-0
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of, as photoactivable probe for sodium-hydroxy ion exchanger)
RN 127513-40-0 CAPLUS
CN Pyrazinecarboxamide, 3-amino-N-(aminoiminomethyl)-5-[4-[4-azido-2-hydroxy-3(or 5)-(iodo-125I)benzoyl]-1-piperazinyl]-6-chloro- (9CI) (CA INDEX NAME)

PAGE 1-A

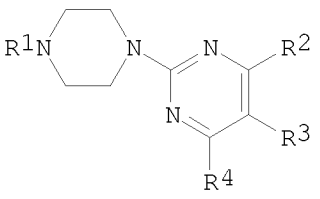


D1— ^{125}I

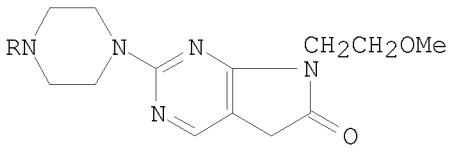
L5 ANSWER 28 OF 41 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1988:473472 CAPLUS
DOCUMENT NUMBER: 109:73472
ORIGINAL REFERENCE NO.: 109:12309a,12312a
TITLE: Preparation of 2-(1-piperazinyl)pyrimidines as agents for treating neuropathy
INVENTOR(S): Awaya, Akira; Nakano, Takuo; Kobayashi, Hisashi; Tan, Kenei; Horikomi, Kazutoshi; Sasaki, Tadayuki; Yokoyama, Keiichi; Ohno, Hiroyasu; Kato, Kozi; et al.
PATENT ASSIGNEE(S): Mitsui Petrochemical Industries, Ltd., Japan; Mitsui Pharmaceuticals, Inc.
SOURCE: PCT Int. Appl., 120 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 8704928	A1	19870827	WO 1987-JP120		19870224
W: JP, US					
RW: CH, DE, FR, GB, IT, NL					
EP 257102	A1	19880302	EP 1987-901652		19870224
EP 257102	B1	19971119			
R: CH, DE, FR, GB, IT, LI, NL					
JP 2561689	B2	19961211	JP 1987-501286		19870224
EP 799617	A2	19971008	EP 1997-103975		19870224
EP 799617	A3	19971112			
R: DE, FR, GB					
US 4959368	A	19900925	US 1987-130533		19871022
CA 1305142	C	19920714	CA 1987-552445		19871123
JP 08325268	A	19961210	JP 1996-148712		19960520
PRIORITY APPLN. INFO.:			JP 1986-37244	A	19860224
			JP 1986-73443	A	19860331
			EP 1987-901652	A3	19870224
			JP 1987-501286	A3	19870224
			WO 1987-JP120	W	19870224

OTHER SOURCE(S): CASREACT 109:73472; MARPAT 109:73472
GI



I



II

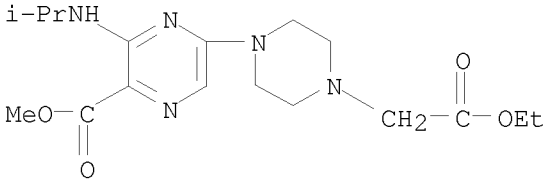
AB The title compds. [I; R1 = H, C2-4 acyl, C2-5 alkoxycarbonyl, C3-5 alkoxycarbonylmethyl, PhCH2, 3,4-(MeO)2C6H3CO, 3,4-methylenedioxybenzyl; R2 = H, NH2, C1-4 alkylamino, C1-5 alkoxy, C2-4 alkoxycarbonyl; R3 = H,

C2-4 alkoxycarbonyl, C1-9 dialkylaminocarbonyl, C1-5 alkoxy, HOCH2CH2; R2R3 = atoms to form a 4- to 7-membered carbocyclic or heterocyclic ring containing N, O or S ; R4 = H, C1-4 alkylthio] were prepared as agents for treating neuropathy. Et 2-(benzylpiperazino)-4-chloropyrimidine-5-acetate (0.08 mol) and 0.16 mol MeOCH2CH2NH2 in EtOH were heated in an autoclave at 150° for 7h to give 65% pyrrolopyrimidine derivative II (R = PhCH2) which was hydrogenated over 10% Pd/C to give .apprx.100% II (R = H) (III). III.HCl in vitro at 1 mμ was approx. twice as potent as isaxonine in promoting growth of mouse neural cells neuro-2a.

IT 115495-88-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, for treatment of neuropathy)

RN 115495-88-0 CAPLUS

CN Pyrazinecarboxylic acid, 5-[4-(2-ethoxy-2-oxoethyl)-1-piperazinyl]-3-[(1-methylethyl)amino]-, methyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 29 OF 41 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1986:607443 CAPLUS
DOCUMENT NUMBER: 105:207443
ORIGINAL REFERENCE NO.: 105:33441a,33444a
TITLE: Inhibition of chemotactic factor-activated sodium/proton exchange in human neutrophils by analogs of amiloride: structure-activity relationships in the amiloride series
AUTHOR(S): Simchowitz, Louis; Cragoe, Edward J., Jr.
CORPORATE SOURCE: Sch. Med., Washington Univ., St. Louis, MO, 63125, USA
SOURCE: Molecular Pharmacology (1986), 30(2), 112-20
CODEN: MOPMA3; ISSN: 0026-895X
DOCUMENT TYPE: Journal
LANGUAGE: English

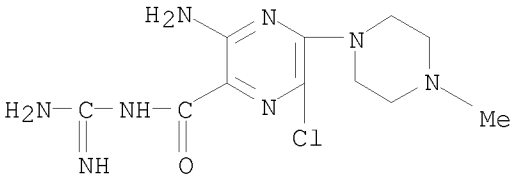
AB The ability of a number of analogs of the diuretic, amiloride, to inhibit chemotactic factor-stimulated Na+/H+ exchange in human neutrophils was investigated. Intracellular pH (pHi) changes were measured from the equilibrium distribution of 14C-labeled 5,5-dimethyloxazolidine-2,4-dione (DMO). Exposure of cells to 10 nM N-formyl-methionyl-leucyl-phenylalanine (FMLP) caused activation of Na+/H+ exchange: in 140 mM Na+ medium (extracellular pH 7.40), the pHi rose from a resting value of .apprx.7.25 to reach a new steady state of .apprx.7.75 by 10-15 min. This intracellular alkalinization was sensitive to amiloride (apparent Ki .apprx.75 μM), a known inhibitor of Na+/H+ countertransport. The structure-activity relationships in the amiloride series were characterized by testing the effect of these compds. on the DMO-derived pHi changes and on the FMLP-stimulated rate of 22Na+ efflux from the cells. Substitutions of the guanidino group of amiloride resulted in relatively inactive products (Ki ≥ 1 mM). Replacement of the 6-Cl group of amiloride by other halogen atoms had only modest effects on drug efficacy. However, replacement of one or both H atoms of the 5-amino group by short alkyl groups led to a 10-500-fold increase in potency for inhibition of Na+/H+ exchange. Amiloride and 3 of its more potent derivs. (compds. I, O, and MM, the 5-N,N-dimethyl, 5-N,N-diethyl and 5-N,N-hexamethylene analogs, resp.) caused parallel inhibition of

FMLP-activated 22Na+ efflux and the rate of intracellular alkalinization, with apparent Ki values of .apprx.75, 8, 1, and 0.2 μM, resp. In each instance, the inhibitory effects of the drugs were readily reversible on washing the cells. None of the compds. altered the binding of 3H-labeled FMLP to its cell surface receptors. The development of potent derivs. of amiloride should provide powerful tools for assessing the role of FMLP-activated Na+/H+ exchange and the resultant pHi transients on stimulated neutrophil functions.

IT 95569-38-3
RL: BIOL (Biological study)
(chemotactic factor-activated cation exchange in human neutrophil inhibition by, structure in relation to)

RN 95569-38-3 CAPLUS

CN Pyrazinecarboxamide, 3-amino-N-(aminoiminomethyl)-6-chloro-5-(4-methyl-1-piperazinyl)- (9CI) (CA INDEX NAME)



L5 ANSWER 30 OF 41 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1985:142785 CAPLUS

DOCUMENT NUMBER: 102:142785

ORIGINAL REFERENCE NO.: 102:22271a,22274a

TITLE: The interaction of amiloride analogs with the sodium/proton exchanger in kidney medulla microsomes

AUTHOR(S): Labelle, Edward F.; Woodard, Peggy L.; Cragoe, Edward J., Jr.

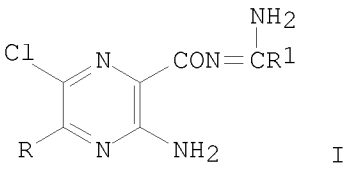
CORPORATE SOURCE: Med. Branch, Univ. Texas, Galveston, TX, 77550, USA

SOURCE: Biochimica et Biophysica Acta, Biomembranes (1984), 778(1), 129-38
CODEN: BBBMBS; ISSN: 0005-2736

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



I

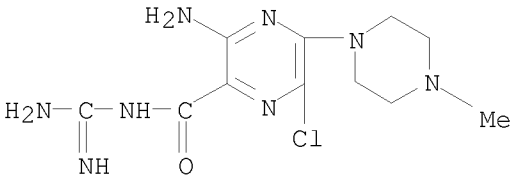
AB The effects of 10 amiloride analogs I (R = NH2, NMe2, NHCHMe2, NHCH2Ph, NPh2, NHCH2CHMe2, etc.; R1 = NH2, NMe2, or NHCH2Ph) on Na+-H+ exchange in rabbit kidney medulla microsomes were examined Most of the analogs appeared to inhibit Na+ uptake into the microsomes more effectively than did amiloride [2609-46-3] either in the presence or absence of a pH gradient. However, the analogs were also capable of stimulating Na+ efflux from the microsomes at concns. somewhat higher than the concns. at which they inhibited Na+ influx. The concns. at which the analogs stimulated Na+

efflux were about 2-4-times higher than the concns. at which they blocked influx. This suggested that the 2 processes were related. The analogs that stimulated efflux most effectively (the 5-N-benzylamino analog [1160-51-6] of amiloride and the 5-N-butyl-N-methylamino analog [1154-79-6]) were shown to induce completely reversible effects. These analogs did not stimulate L-[3H]glucose efflux from medulla microsomes which ruled out nonspecific vesicle destruction or reversible detergent effects. These analogs also induced Na+ efflux from microsomes in the presence of high concns. of added buffer, which ruled out weak base-uncoupling effects. The possibility exists that these analogs are carried into the microsomes via the Na+-H+ exchange protein and that this permits them to both block Na+ influx into the microsomes and stimulate Na+ efflux as well.

IT 95569-38-3
RL: BIOL (Biological study)
(kidney medulla microsome sodium and proton exchange response to)

RN 95569-38-3 CAPLUS

CN Pyrazinecarboxamide, 3-amino-N-(aminoiminomethyl)-6-chloro-5-(4-methyl-1-piperazinyl)- (9CI) (CA INDEX NAME)



L5 ANSWER 31 OF 41 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1976:31120 CAPLUS
DOCUMENT NUMBER: 84:31120
ORIGINAL REFERENCE NO.: 84:5097a,5100a
TITLE: Pyrazinecarboxamide derivatives
INVENTOR(S): Murakami, Masuo; Takahashi, Kozo; Hirata, Yasuhumi; Takashima, Mutsuo; Takeda, Masaaki; Ino, Hiroyoshi; Iwanami, Sumio
PATENT ASSIGNEE(S): Yamanouchi Pharmaceutical Co., Ltd., Japan
SOURCE: Ger. Offen., 62 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2461802	A1	19750717	DE 1974-2461802	19741230
DE 2461802	C2	19850103		
JP 50105675	A	19750820	JP 1974-7726	19740116
JP 55050944	B	19801220		
JP 50140468	A	19751111	JP 1974-43027	19740416
AU 7476649	A	19760624	AU 1974-76649	19741219
US 4041032	A	19770809	US 1974-534636	19741219
SE 7416137	A	19750717	SE 1974-16137	19741220
SE 420602	B	19811019		
SE 420602	C	19820128		
DK 7406730	A	19750908	DK 1974-6730	19741220
DK 139846	B	19790430		
DK 139846	C	19791008		
AT 7410288	A	19770415	AT 1974-10288	19741223

AT 340437	B	19771212			
GB 1484049	A	19770824	GB 1974-55539		19741223
FR 2257293	A1	19750808	FR 1974-42978		19741227
FR 2257293	B1	19800208			
BE 824005	A1	19750630	BE 1974-152061		19741230
NL 7417060	A	19750718	NL 1974-17060		19741231
CA 1050540	A1	19790313	CA 1975-217443		19750107
PRIORITY APPLN. INFO.:			JP 1974-7726	A	19740116
			JP 1974-43027	A	19740416

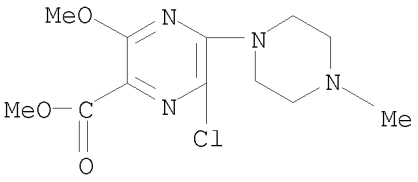
GI For diagram(s), see printed CA Issue.

AB Pyrazinecarboxamides I (R = H, R1 = substituted aminoalkyl, N-alkyl-2-pyrrolidinylmethyl, N-alkyl-3-piperidinyl; NRR1 = substituted piperidino, piperazino; R2 = H, NH2, substituted amino, OMe, SMe, OC6H4OMe-2, Me) (38 compds.) were prepared by aminating II (R3 = H, alkyl, R4 = Cl). Thus II (R2 = R4 = H, R3 = Me) was chlorinated, II (R2 = R4 = Cl, R3 = Me) aminated, and II (R2 = NH2, R3 = Me, R4 = Cl) treated with 2-aminomethyl-1-ethylpyrrolidine to give I (R = H, R1 = 1-ethyl-2-pyrrolidinylmethyl, R2 = NH2), which had an antiemetic ED50 of 2γ/kg s.c. in dogs.

IT 57796-29-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and amination of)

RN 57796-29-9 CAPLUS

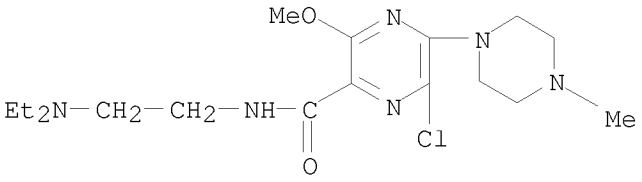
CN Pyrazinecarboxylic acid, 6-chloro-3-methoxy-5-(4-methyl-1-piperazinyl)-, methyl ester (9CI) (CA INDEX NAME)



IT 57796-32-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 57796-32-4 CAPLUS

CN Pyrazinecarboxamide, 6-chloro-N-[2-(diethylamino)ethyl]-3-methoxy-5-(4-methyl-1-piperazinyl)- (9CI) (CA INDEX NAME)



L5 ANSWER 32 OF 41 CAPLUS COPYRIGHT 2008 ACS on STN

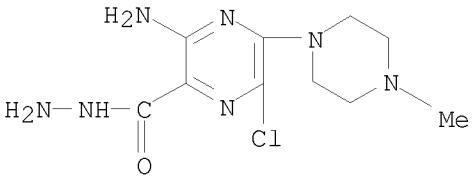
ACCESSION NUMBER:	1973:487342 CAPLUS
DOCUMENT NUMBER:	79:87342
ORIGINAL REFERENCE NO.:	79:14115a,14118a
TITLE:	6-Substituted 5-chloro-1,3-dihydro-2H-imidazo[4,5-b]pyrazin-2-ones with hypotensive activity
AUTHOR(S):	Jones, James H.; Holtz, Wilbur J.; Cragoe, Edward J., Jr.
CORPORATE SOURCE:	Merck Sharp and Dohme Res. Lab. Div., Merck and Co.,

Inc., West Point, PA, USA
SOURCE: Journal of Medicinal Chemistry (1973), 16(5), 537-42
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English

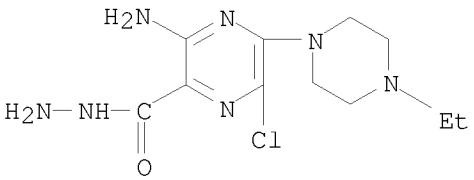
AB Title compds. substituted in the 6 position with alkylamino, dialkylamino, alkylaminoethylamino, or pyridylalkylamino groups were potent hypotensive agents in dogs because of the peripheral vasodilatatory properties. Most were also inhibitors of beef heart cyclic AMP phosphodiesterase [9036-21-9] in vitro. Thus, 5-chloro-6-ethylamino-1,3-dihydro-2H-imidazo[4,5-b]pyrazin-2-one (I) [27604-23-5] at 20 mg/kg i.v. produced >50 mm Hg decrease in carotid arterial blood pressure in anesthetized dogs, and at 10-3 M produced 70% inhibition of cyclic AMP phosphodiesterase in vitro. Most compds. also possessed bronchodilatatory and cardiac stimulant properties. 5-Chloro-6-[[2-(dimethylamino)ethyl]amino]-1,3-dihydro-2H-imidazo[4,5-b]pyrazin-2-one [27604-38-2] produced hypotension and bronchodilation, but had no cardiac stimulant properties and was a poor inhibitor of cyclic AMP phosphodiesterase. To synthesize I, 3-amino-5,6-dichloropyrazine-2-carboxylic acid Me ester was converted to the 5-ethylamino derivative by the method of K. L. Shepard, et al. (1969), converted to the hydrazide, then to the azide, and submitted to thermal Curtius rearrangement with intramol. cyclization.

IT 27250-90-4P 27250-91-5P 27282-33-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

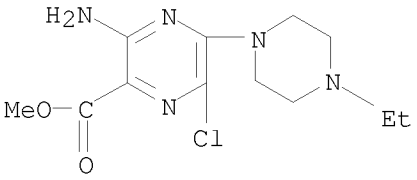
RN 27250-90-4 CAPLUS
CN Pyrazinecarboxylic acid, 3-amino-6-chloro-5-(4-methyl-1-piperazinyl)-, hydrazide (8CI, 9CI) (CA INDEX NAME)



RN 27250-91-5 CAPLUS
CN Pyrazinecarboxylic acid, 3-amino-6-chloro-5-(4-ethyl-1-piperazinyl)-, hydrazide (8CI, 9CI) (CA INDEX NAME)



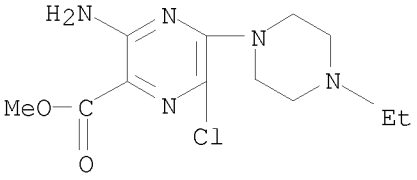
RN 27282-33-3 CAPLUS
CN Pyrazinecarboxylic acid, 3-amino-6-chloro-5-(4-ethyl-1-piperazinyl)-, methyl ester (8CI, 9CI) (CA INDEX NAME)



L5 ANSWER 33 OF 41 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1971:125730 CAPLUS
DOCUMENT NUMBER: 74:125730
ORIGINAL REFERENCE NO.: 74:20315a,20318a
TITLE: Amine imides of pyrazine derivatives
INVENTOR(S): Grabowski, Edward J. J.; Tristam, Edward W.; Tull, Roger J.
PATENT ASSIGNEE(S): Merck and Co., Inc.
SOURCE: Ger. Offen., 17 pp. Division of Ger. Offen. 1,957,711
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 1965989	A	19710218	DE 1969-1965989	19691117
US 3567725	A	19710302	US 1968-777478	19681120
NL 6915957	A	19700522	NL 1969-15957	19691022
GB 1246006	A	19710915	GB 1969-1246006	19691117
BE 741910	A	19700519	BE 1969-741910	19691119
AT 290528	B	19710611	AT 1969-10825	19691119
ZA 6908081	A	19710728	ZA 1969-8081	19691119
BR 6914329	D0	19730222	BR 1969-214329	19691119
FR 2035817	A5	19701224	FR 1969-39941	19691120
FR 2035817	B1	19730112		

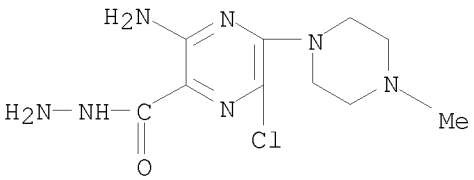
PRIORITY APPLN. INFO.: US 1968-777478 A 19681120
GI For diagram(s), see printed CA Issue.
AB The title compds. (I), useful as intermediates for the preparation of pharmaceutical imidazo[4,5-b]pyrazin-2-ones, were prepared by reaction of II (X = Cl) with RR1NH in an alc. at reflux temperature via II (X = NRR1) (II), which were added to R3-substituted alkylene oxide and refluxed with H2NNR22 in MeOH. Among 25 pyrazines prepared were III (R and R1 given): Et, H (IV); HC.tplbond.CCH2, H; MeO(CH2)2, H; iso-PrNH(CH2)3, H; 3-morpholinopropyl, H; Pr, Me; Et2N(CH2)2, Me. Reaction of IV, propylene oxide, and H2NNMe2 gave I (R = Et, R1 = H, R2 = R3 = Me).
IT 27282-33-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 27282-33-3 CAPLUS
CN Pyrazinecarboxylic acid, 3-amino-6-chloro-5-(4-ethyl-1-piperazinyl)-, methyl ester (8CI, 9CI) (CA INDEX NAME)



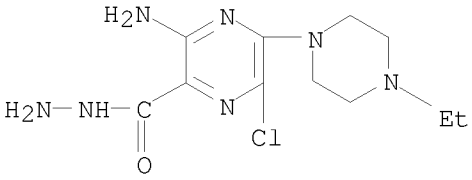
L5 ANSWER 34 OF 41 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1970:509796 CAPLUS
DOCUMENT NUMBER: 73:109796
ORIGINAL REFERENCE NO.: 73:17879a,17882a
TITLE: Diuretic 1-(3-amino-2-pyrazinylcarboxyl) semicarbazides and -thiosemicarbazides
INVENTOR(S): Cragoe, Edward J., Jr.; Bicking, John B.; Shepard, Kenneth L.
PATENT ASSIGNEE(S): Merck and Co., Inc.
SOURCE: Ger. Offen., 61 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 1956891	A	19700611	DE 1969-1956891	19691112
US 3555024	A	19710112	US 1968-775543	19681113
NL 6915953	A	19700515	NL 1969-15953	19691022
FR 2024847	A1	19700904	FR 1969-38784	19691112

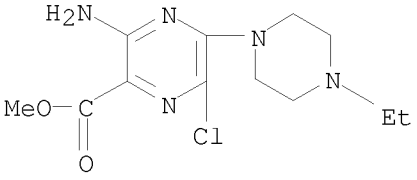
PRIORITY APPLN. INFO.: US 1968-775543 A 19681113
GI For diagram(s), see printed CA Issue.
AB The title compds. (.apprx.100) I, (X = S or O; R1 in most cases an amino group), which have saluretic and diuretic properties, were prepared from isothiocyanates or cyanates and hydrazides; the latter were prepared from substituted Me 3-aminopyrazinecarboxylates and hydrazine. Thus, Me 5,6-dichloro-3-aminopyrazinecarboxylate was treated with M2NH to give Me 3-amino-5-dimethylamino-6-chloropyrazinecarboxylate, which was heated with NH2NH2.H2O in EtOH to obtain the hidrazide (II). II was heated in C5H5N or MeCN with H2C:CHCH2NCO to give I (R = H2C:CHCH2, R1 = Me2N, R2 = Cl, X = O). Heating II with H2C:CHCH2NCS in AcOH gave I (R = H2C:CHCH2, R1 = Me2N, R2 = Cl, X = S). Other R groups were Ph, Me, Pr, and Bu, and other R1 groups were Me3CNH, piperidinoamino, and 2-(2-pyridyl)hydrazino.
IT 27250-90-4P 27250-91-5P 27282-33-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 27250-90-4 CAPLUS
CN Pyrazinecarboxylic acid, 3-amino-6-chloro-5-(4-methyl-1-piperazinyl)-, hydrazide (8CI, 9CI) (CA INDEX NAME)



RN 27250-91-5 CAPLUS
CN Pyrazinecarboxylic acid, 3-amino-6-chloro-5-(4-ethyl-1-piperazinyl)-, hydrazide (8CI, 9CI) (CA INDEX NAME)



RN 27282-33-3 CAPLUS
CN Pyrazinecarboxylic acid, 3-amino-6-chloro-5-(4-ethyl-1-piperazinyl)-, methyl ester (8CI, 9CI) (CA INDEX NAME)

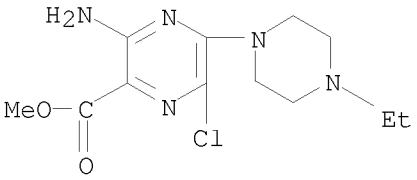


L5 ANSWER 35 OF 41 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1970:466621 CAPLUS
DOCUMENT NUMBER: 73:66621
ORIGINAL REFERENCE NO.: 73:10915a,10918a
TITLE: 5-Amino-6-chloroimidazo[4,5-b] pyrazin-2(3H)-ones
INVENTOR(S): Grabowski, Edward J. J.; Tristram, Edward W.; Tull, Roger J.
PATENT ASSIGNEE(S): Merck and Co., Inc.
SOURCE: Ger. Offen., 30 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 1957711	A	19700618	DE 1969-1957711	19691117
US 3567725	A	19710302	US 1968-777478	19681120
NL 6915957	A	19700522	NL 1969-15957	19691022
GB 1246006	A	19710915	GB 1969-1246006	19691117
BE 741910	A	19700519	BE 1969-741910	19691119
AT 290528	B	19710611	AT 1969-10825	19691119
ZA 6908081	A	19710728	ZA 1969-8081	19691119
BR 6914329	D0	19730222	BR 1969-214329	19691119
FR 2035817	A5	19701224	FR 1969-39941	19691120
FR 2035817	B1	19730112		

PRIORITY APPLN. INFO.: US 1968-777478 A 19681120
GI For diagram(s), see printed CA Issue.
AB The title compds. (I), prepared through the intermediate esters (II) and aminoimides (III), are orally active, antihypertensive, diuretic, and saluretic drugs of low toxicity pharmaceutical prepns. are related. R2 is H, Me, or Et. R1 is, e.g., 2-propynyl, MeO(CH2)2, 2-pyridylmethyl, 3-pyridylmethyl, or AcNH(CH2)2. Forty-two examples appear.
IT 27282-33-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 27282-33-3 CAPLUS
CN Pyrazinecarboxylic acid, 3-amino-6-chloro-5-(4-ethyl-1-piperazinyl)-,

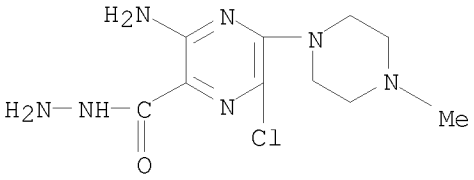
methyl ester (8CI, 9CI) (CA INDEX NAME)



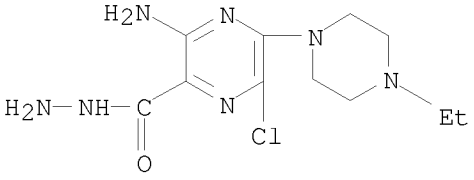
L5 ANSWER 36 OF 41 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1970:435403 CAPLUS
DOCUMENT NUMBER: 73:35403
ORIGINAL REFERENCE NO.: 73:5869a,5872a
TITLE: Diuretic and saluretic 1-(3,5-diamino-6-chloropyrazinecarbonyl)-3-methyl-3-thioisosemicarbazides
INVENTOR(S): Cragoe, Edward J., Jr.; Shepard, Kenneth L.
PATENT ASSIGNEE(S): Merck and Co., Inc.
SOURCE: Ger. Offen., 75 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 1956859	A	19700604	DE 1969-1956859	19691112
US 3555023	A	19710112	US 1968-775542	19681113
NL 6915952	A	19700515	NL 1969-15952	19691022
FR 2024846	A1	19700904	FR 1969-38783	19691112

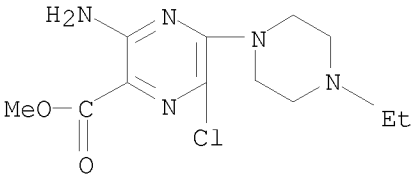
PRIORITY APPLN. INFO.: US 1968-775542 A 19681113
GI For diagram(s), see printed CA Issue.
AB The diuretic and saluretic title compds. (I) were prepared Thus, 6.06 g 3,5-diamino-6-chloropyrazinecarboxylic hydrazide, prepared by refluxing the Me ester with H2NNH2, and 3.3 g KSCN in HOAc was heated 2 hr on a steam bath to give 2.19 g 1-(3,5-diamino-6-chloropyrazinecarbonyl)thiosemicarbazide (II). MeI in EtOH was added to 6.0 g II in 0.5N NaOH and stirred 30 min to give 3.68 g I (R = R1 = H) (Ia). Similarly prepared were I (R = H, R1 = Me2NCH2CH2) and 79% I (R = CH2:CHCH2, R1 = H). Reaction of 3,5-diamino-6-chloropyrazinecarboxylic acid with N-tertbutyl-5-methylisoxazolium perchlorate 2 hr in HCONMe2 in the presence of Et3N gave 87% N-tert-butyl - 3 - methyl - 3 - (3,5-diamino-6-chloropyrazinecarbonyloxy)acrylamide. This (3.27 g) was added to 5.11 g H2NN:C(SMe)-NH2.HI and Na in iso-PrOH and refluxed 2 hr to give 0.30 g Ia. Capsules were prepared containing 500 mg Ia and 5 mg Mg stearate.
IT 27250-90-4P 27250-91-5P 27282-33-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 27250-90-4 CAPLUS
CN Pyrazinecarboxylic acid, 3-amino-6-chloro-5-(4-methyl-1-piperazinyl)-, hydrazide (8CI, 9CI) (CA INDEX NAME)



RN 27250-91-5 CAPLUS
CN Pyrazinecarboxylic acid, 3-amino-6-chloro-5-(4-ethyl-1-piperazinyl)-, hydrazide (8CI, 9CI) (CA INDEX NAME)



RN 27282-33-3 CAPLUS
CN Pyrazinecarboxylic acid, 3-amino-6-chloro-5-(4-ethyl-1-piperazinyl)-, methyl ester (8CI, 9CI) (CA INDEX NAME)



L5 ANSWER 37 OF 41 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1970:111514 CAPLUS
DOCUMENT NUMBER: 72:111514
ORIGINAL REFERENCE NO.: 72:20155a,20158a
TITLE: Imidazopyrazinones
INVENTOR(S): Cragoe, Edward J., Jr.; Jones, James Holden
PATENT ASSIGNEE(S): Merck and Co., Inc.
SOURCE: Fr., 49 pp.
CODEN: FRXXAK
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 1578366		19690814	FR	19680808
DE 1795062			DE	
GB 1193035			GB	
US 3507866		19700421	US	19680509
ZA 6805115		19680000	ZA	
PRIORITY APPLN. INFO.:			US	19670808
			US	19680509

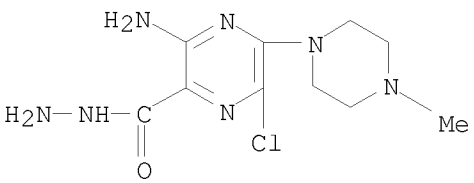
OTHER SOURCE(S): MARPAT 72:111514
GI For diagram(s), see printed CA Issue.
AB 1H-Imidazo[4,5-b]pyrazin-2-ones (I) are prepared by heating in a solvent the

corresponding pyrazinoic acid azides, obtained by diazotizing 3-aminopy razinoic acid hydrazides (II), prepared by treatment of III with N2H4. Thus, 178 g Me 3-amino-5,6-dichloropyrazinoate (IV) in 1.1 l. iso-PrOH stirred with addition of 200 g Me2NH in 2 l. iso-PrOH and the mixture refluxed 1 hr yielded 97% III (R = H, R1 = R2 = Me, R3 = Cl), m. 145.5-6.5°. III (R = H, R1 = R2 = Me, R3 = Cl) (V) in 100 ml 48% HBr and 200 ml AcOH at 5° added to 15 ml Br in 30 ml AcOH and the mixture stirred 30 min at 5° with 17 g NaNO2 in 30 ml H2O, treated at 10° with 45 g NaHSO3 in 150 ml H2O gave Me 3-bromo-5-dimethylamino-6-chloropyrazinoate, m. 98-9° (C6H12). V (11.8 g) heated 30 min on a steam bath in 30 ml Me2SO containing 4.88 g H2NCH2CH2OH gave III (R = HOCH2CH2, R2 = R3 = Me, R3 = Cl), m. 103-5° (BuCl). V heated 1.5 hr on a steam bath with 70% EtNH2 in Me2SO yielded 92% III (R = Et, R1 = R2 = Me, R3 = Cl) m. 93-5°. II (R = H, R1 = R2 = Me, R3 = Cl) (15.0 g) in 150 ml 0.5N HCl stirred with addition of 4.5 g NaNO2 in 10 ml H2O and the dried precipitated azide refluxed 20 hr in 200 ml absolute alc. yielded 35% I (R = H, R2 = R1 = Me, R3 = Cl), m. 216-17° (decomposition) (AcOEt-C6H14). I (R = R2 = H, R1 = Et, R3 = Cl) (Va) (2.1 g) in 250 ml MeOH hydrogenated at 20° and 2.1 kg/sq. cm in the presence of 2 g 5% Pd-C and 2.0 g MgO yielded 44% 5-ethylamino-1H-imidazo[4,5-b]pyrazin-2-one, m. 250-2° (decomposition). This (3 g) and 4 g NaOAc.3H2O in 20 ml AcOH treated slowly with 0.9 ml Br and the precipitate crystallized from dilute alc. gave I (R = R1 = H, R2 = Et, R3 = Br).

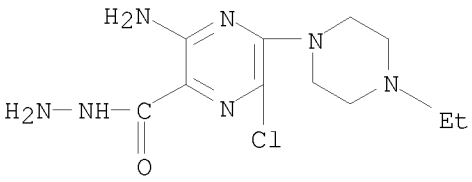
Va (2.1 g) in 25 ml DMF and 1.4 ml NEt3 stirred 30 min at 20° with addition of 2.2 g ClCO2Et and the solution poured into 100 ml H2O yielded the 1,3-bis(ethoxycarbonyl) derivative, m. 202-4°. Va refluxed 3 hr in Ac2O gave the corresponding 1,3-di-Ac compound, m. 198-200°. II (R = Et, R1 = R2 = Me, R3 = Cl) (8 g) in 15 ml 6N HCl treated dropwise at 10° with 2.14 g NaNO2 in 20 ml H2O with vigorous stirring 45 min and the dried precipitated azide [7.8 g, m. 110° (decomposition)] heated 1 hr in MeOCH2CH2OH on a steam bath gave 1-ethyl-5-chloro-6-dimethylamino-1H-imidazo[4,5-b]-pyrazin-2-one, m. 175-8°. IV (11.1 g) in 100 ml MeOCH2-CH2OH heated 1.5 hr on a steam bath with 50 ml 64% N2H4 and cooled yielded 3-amino-5-hydrazino-6-chloropyrazinoic acid hydrazide, m. 238-9° (decomposition). This (5.3 g) in 200 ml 5% HCl treated dropwise with 3.36 g NaNO2 in 10 ml H2O and the dried azide heated 2 hr in 100 ml EtOCH2CH2OH on a steam bath yielded 81% 5-azido-6-chloro-1H-imidazo[4,5-b]pyrazin-2-one, m. 188° (decomposition). Formulations for cachets and aerosols are given. A large number (>100) of other intermediates and I are prepared I are prepared primarily as antihypertensive agents with some diuretic and saluretic effects, but other pharmacol. properties are also listed.

IT 27250-90-4P 27250-91-5P 27282-33-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

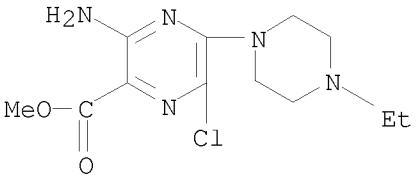
RN 27250-90-4 CAPLUS
CN Pyrazinecarboxylic acid, 3-amino-6-chloro-5-(4-methyl-1-piperazinyl)-, hydrazide (8CI, 9CI) (CA INDEX NAME)



RN 27250-91-5 CAPLUS
CN Pyrazinecarboxylic acid, 3-amino-6-chloro-5-(4-ethyl-1-piperazinyl)-, hydrazide (8CI, 9CI) (CA INDEX NAME)



RN 27282-33-3 CAPLUS
CN Pyrazinecarboxylic acid, 3-amino-6-chloro-5-(4-ethyl-1-piperazinyl)-, methyl ester (8CI, 9CI) (CA INDEX NAME)



L5 ANSWER 38 OF 41 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1968:436172 CAPLUS
DOCUMENT NUMBER: 69:36172
ORIGINAL REFERENCE NO.: 69:6762h,6763a
TITLE: (3-Amino-2-pyrazinecarbonyl)guanidines
INVENTOR(S): Cragoe, Edward J., Jr.
PATENT ASSIGNEE(S): Merck and Co., Inc.
SOURCE: U.S., 26 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3313813		19670411	US 1963-313315	19621030
DE 1795438			DE	

GI For diagram(s), see printed CA Issue.
AB Title compds. I are prepared from II, III, and IV. Thus, 3318 g. SO2Cl2 is added in 30 min. to 765 g. Me 3-amino-2-pyrazinecarboxylate in 5.1 C6H6; the mixture is agitated 1 hr., refluxed 5 hrs., and agitated overnight to give 724 g. Me 3-amino-5,6-dichloropyrazinecarboxylate (V), m. 233-4° (MeCN). A mixture of 100 g. V. and 1.1 Me2SO is heated to 65° and NH3 gas is introduced into the mixture in 45 min. at 65-70°; the mixture is cooled to 10° and NH3 is introduced in 1.25 hrs. to give 91.5% Me 3,5-diamino-6-chloropyrazinecarboxylate, m. 212-13° (MeCN). Also prepared, by known methods are the following II (X, Y, Z, and m.p. given): MeO, NH2, H, 252-4° (decomposition); MeO, NH2, Br, 217-19°; MeO, NH2, iodine, 200-2°; MeO, PhNH, Cl, 171.5-73°; MeO, p-ClC6H4NH, Cl, 207-8°; MeO, Me2N, Cl, 145.5-6.5°; MeO, MeS, Cl, 214-16°; MeO, MeSO, Cl, 237.5-40.5° (decomposition); MeO, OH, Cl, .apprx.245° (decomposition); MeO, OH, H, 220-60° (decomposition); MeO, NH2,H, 252-4° (decomposition); MeO, Me2N, H, 242.5-3.5°; MeO, MeO, H, 205.5-7.5°; MeO, PhCH2NH, H, 157-8°; MeO, MeO, MeO, Cl, 255-7°; MeO, MeS, Cl, 212-14°; MeO, SH, Cl, 207-8° (decomposition); MeO,EtO, Cl, 123-5°; MeO, H, Me, 138.5-40.5°;

MeO, Cl, Me, 176.5-9.5°; MeO, Me2N, Me, 108.5-10.5°; MeO, Me, H, 165-7°; MeO, Me, Br, 179-81°; NH2, H, Et, 165.5-8.5°; OH, H, Et, 149-52°; MeO, H, Et, 85-7.5°; OH, cyclohexyl, H, 182.5-3.5°; MeO, cyclohexyl, H, 173-4.5°; NH2, H, cyclohexyl, -; OH, H, cyclohexyl, -; MeO, H, cyclohexyl, 126.5-8.0°; NH2, H, cyclopropyl, 185.5-7.5°; OH, H, cyclopropyl, 169-72°; MeO, H, cyclohexyl, 112.5-14.5°; MeO, Ph, H, 231-2°; MeO, H, Ph, 140-1°; MeO, Cl, Ph, 187.5-91.5°; MeO, Ph, Br, 217-21°; OH, H, p-ClC6H4, 213-15°; MeO, H, p-ClC6H4, 181.5-3.5°; MeO, Cl, Ph, 187.5-90.5°; MeO, Me2N, Ph, 167-9.5°; MeO, H, Cl, 142° (decomposition); MeO, MeHN, Cl, 221-2°; MeO, EtNH, Cl, 149-50°; MeO, PrNH, Cl, 138-40°; MeO, iso-PrNH, Cl, 125.5-6.5°; MeO, CH2:CHCH2NH, Cl, 105-6.5°; MeO, BuNH, Cl, 140-2°; MeO, sec-BuNH, Cl, 106-8°; MeO, iso-BuNH, Cl, 113.5-15.5°; MeO, tert-BuNH, Cl, 98-108°; MeO, Me(CH2)4NH, Cl, 100.5-2.5°; MeO, BuCHMeNH, Cl, -; MeO, Et2CHNH, Cl, -; MeO, Me(CH2)5NH, Cl, 72.5-5.5°; MeO, cyclopropylmethylamino, Cl, 132-3°; MeO, cyclopropylamino, Cl, 167-9°; MeO, cyclopentylamino, Cl, 119.5-21.5°; MeO, PhCH2NH, Cl, 157-8°; MeO, p-MeC6H4CH2NH, Cl, 112.5-14.5°; MeO, o-FC6H4CHNH, Cl, 171-4°; MeO, p-ClC6H4CH2NH, Cl, 136-7°; MeO, PhCH2CH2NH, Cl, 115-19°; MeO, F3CCH2NH, Cl, 153-4°; MeO, F3CCH2CH2NH, Cl, 124.5-5.5°; MeO, HOCH2CH2NH, Cl, 155-7°; MeO, HOCH2(CHOH)4CH2NH, Cl, 172-5°; MeO, H2NCH2CH2NH, Cl, 265°; MeO, Me2NCH2CH2NH, Cl, 257°; MeO, 4-pyridylmethylamino, Cl, 95-7°; Me, 2-furylmethylamino, Cl, 148-9°; MeO, MeEtN, Cl, 102-4°; MeO, MePrN, Cl, 83.5-5.5°; MeO, iso-PrMeN, Cl, 75.5-7.5°; MeO, Me(CH2:CHCH2)N, Cl, 90.5-2°; MeO, MeBun, Cl, 59.5-61.5°; MeO, Et2N, Cl, 99-101°; MeO, EtPrN, Cl, -; MeO, iso-PrEtN, Cl, -; MeO, Et(CH2:CHCH2)N, Cl, -; MeO, EtBun, Cl, 77.5-9.5°; Me, Pr2N, Cl, 68.5-71.5°; MeO, PrBuN, Cl, -; MeO, 1-pyrrolidinyl, Cl, 168-71°; MeO, hexamethylenimino, Cl, 109-11°; MeO, 4-methylpiperazino, Cl, 186-8°; MeO, MeNHNH, Cl, 136.5-8°; MeO, Me2NCH2CH2O, Cl, 134.5-6.5°; NH2, H, Cl, 227-30°; OH, H, MeSO2, 239-42° (decomposition).

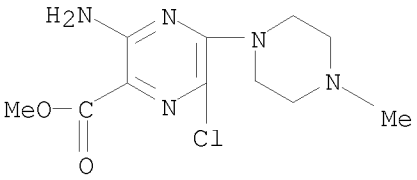
p-Methylbenzylamine is treated with H2NC(:NH)SMe.0.5H2SO4 to give 28% p-MeC6H4CH2NHC(:NH)NH2HCl, m. 153-5°. Similarly prepared are Me(PhCH2)NC(:NH)NH2.HCl, m. 122.5-5.5°, and the following RNHC(:NH)NH2.HCl (R and m.p. given): o-ClC6H4CH2, 131-6°; p-ClC6H4CH2, 162.5-4.5°; p-MeOC6H4CH2, 132-7°; 2,4-Me2C6H3CH2, 105-15°; 2,4-Cl2C6H3CH2, 145-8°; 3,4-Cl2C6H3CH2, 153-7°; PhCH2CH2, 135-8°; PhCH2, 175-8°. 5,6-Diaminouracil-HCl (17.9 g.) is treated at 60° with 14.9 g. cyclohexylglyoxal-0.5H2O to give 7.5 g. 7-cyclohexyllumazine [III (X = H, Y = cyclohexyl)], m. 229-31°, which is hydrolyzed to give II (X = OH, Y = cyclohexyl, Z = H). Similarly prepared are (m.p. given): III (X = Me, Y = Ph) [or III (X = Me, Y = Me)], 281.5-2.5°; III (X = Ph, Y = Me) [or III (X = Me, Y = Ph) [sic], 254.5-5.5°; II (X = OH, Y = Ph, Z = Me) [or II (X = OH, Y = Me, Z = Ph)], 193.5-4.5°; II (X = OH, Y = Me, Z = Ph) [or II (X = OH, Y = Ph, Z = Me)] [sic], 155-6°. II (X = MeO, Y = Ph, Z = Me) [or II (X = MeO, Y = Me, Z = Ph)] (m. 163-4°) and II (X = MeO, Y = Me, Z = Ph) [or II (X = MeO, Y = Ph, Z = Me)][sic] (m. 162.5-3.5°) are prepared by esterification. Methyl 3-isopropylidenamino-6-anilino-2-pyrazinecarboxylate, m. 195.5-7.5°, is prepared from Me2CO and the amine. Me 3-amino-5,6,7,8-tetrahydroquinoxaline-2-carboxylate, m. 154-5°, and Me 3-amino-7-chloroquinoxaline-2-carboxylate, m. 224.5-5.5°, are prepared by esterification. Alloxan-H2O (61.44 g.) is treated with 60 g. 3,4-(H2N)2C6H3Cl to give 33% 8-chloroalloxazine, m. 365-6°, and 42% 7-Chloroalloxazine, m. >380°, which is treated at 165° with NH3 in an autoclave to give 68%

3-amino-7-chloroquinoxaline-2-carboxylic acid, m. 191-2° (decomposition). A mixture of 33 g. II (X = NH2, Y = H, Z = Cl), 200 ml. Ac2O, and 200 ml. HC(OEt)3 is refluxed 1.5 hrs. to give 20 g. 4-hydroxy-6-chloropteridine (VI), m. 268-70° (decomposition). VI (5.5 g.) is treated with 4.4 g. PhCH2SH to give 5.5 g. 4-hydroxy-6-benzylthiopteridine (VIII), m. 233-5°. Similarly prepared is 4-hydroxy-6-methylthiopteridine, m. 289.5-91.5°. VII is heated with NaOH to give II (X = OH, Y = H, Z = PhCH2S(VIII), m. 138.9°. Similarly prepared is II (X = OH, Y = H, Z = MeS), m. 182-4° (decomposition). II (X = MeO, Y = Me2N, Z = Cl) (11.5 g.) is treated with 26.3 g. H2NC(:NH)NH2.HCl (IX) in the presence of 5.75 g. Na to give 93% (3-amino-5-dimethylamino-6-chloro-2-pyrazinecarbonyl)guanidine (X), m. 216-17°, HCl salt m. 298° (decomposition). Similarly prepared is I.HCl (R = R1 = H, X = Y = Cl) (m. 259-61°) which is treated with Me2NH to give X. II (X = MeO, Y = Me2NCH2CHO, Z = Cl) (9.4 g.) is treated with 20.0 g. IX in the presence of 4 g. Na to give 2.5 g. I.2HCl [R = R1 = H, X = NHC(:NH)NH2, Z = Cl], m. >340°. A solution of 8.5 5. VIII in 50 ml. Ac2O is heated 5 hrs. to give 6.6 g. 2-methyl-6-benzylthio-4H-pyrazine[2,3-d][1,3]oxazin-4-one [IV (X = PhCH2S)] (XI), m. 116.5-18.5°; similarly prepared is IV (X = MeS), m. 189-91°. XI (3.4 g.) is treated with 5.0 g. IX in the presence of 1.0 g. Na to give 1.1 g. I (R = R1 = X = H, Y = PhCH2S), m. 171-3° (decomposition). Also prepared, by the above or related methods, are the following I (R = R1 = H) (X, Y, and m.p. given): NH2, Br, 232.5-5.5° (decomposition); NH2, iodine, 273-4° (decomposition); H, MeS, 203-5°; H, MeSO2, 224-6° (decomposition); OH, H, >310°; NH2, H, 286-8°; Me2N, H, 224-5°; MeO, H, 229-30°; PhCH2NH, H, 231-3°; the following I (R = R1 = H, Y, = Cl) (X and m.p. given): NH2, 240.5-1.5° (HCl salt m. 293.5°); MeNH, 238-9°; EtNH, 217-18°; PrNH, 221-2°; iso-PrNH, 215°; CH2:CHCH2NH, 213-14°; BuNH, 219.5°; sec-BuNH, 208-9°; iso-BuNH, 221°; tert-BuNH, 222-3°; Me(CH2)4NH, 215-16°; BuCHMeNH, 186.5-8.5°; Et2CHNH, 209-11°; Me(CH2)5NH, 194.5-6.5°; cyclopropylmethylamino, 220-1.5°; cyclopropylamino, 213-15°; cyclopentylamino, 219-20°; PhCH2NH, 206-9°; p-MeC6H4CH2NH, 216-17°; o-FC6H4CH2NH, 206-8°; p-ClC6H4CH2NH, 225-6°; PhCH2CH2NH, - (HCl salt m. 199-202°); F3CCH2NH, 232-3°; F3CCH2CH2NH, 221-2.5°; HOCH2CH2NH, - (HCl salt m. 272-3°); HOCH2(CHOH)4CH2NH, 223-4°; H2NCH2CH2NH, - (HCl salt m. 311°); Me2NCH2CH2NH, 192.5-4.5°; 4-pyridylmethylamino, 239-40°; 2-furylmethylamino, 217-18°; PhNH, 246.5-8.5°; p-ClC6H4NH, 276-8°; MeEtN, 229-3°; MeBuN, 214-15°; iso-PrMeN, 207-8°; Me(CH2:CHCH2)N, 207-8°; MeBuN, 208-9°; Et2N, 215°; EtPrN, 224-5°; iso-PrEtN, 207-8°; Et(CH2:CHCH2)N, 208-9°; EtBuN, 200.5-1.5°; Pr2N, 221-2°; PrBuN, 215-17°; 1-pyrrolidinyl, 244.5-5.5°; hexamethylenimino, 224-5°; 4-methylpiperazino, - (2HCl salt m; 229-300°); MeNHNH, 234°; Cl2N, - (HCl salt m. 259-61°); MeNH, 218-19° (decomposition); Me2NNMe, - [2HCl salt m. 262° (decomposition)]; MeNH, 210° (decomposition) [sic]; Me2N, 245° (decomposition); MeBrN, - [HCl salt m. 288° (decomposition)]; EtNH, 207.5-9.5° (decomposition); cyclohexylamino, 221-2° (decomposition); cycloheptylamino, 228-30° (decomposition); cyclopropylamino, 196.5-9° (decomposition); PhNH, 224-6° (decomposition); PhNH, 194.5-5.5° (decomposition)[sic]; Ph2N, 234.5-5.5°; PhClN, 214-16° (decomposition); PhBrN, 234-6° (decomposition); p-ClC6H4NH, 282-5° (decomposition); MePhN, 212-13° (decomposition); MePhN, 218-19° (decomposition)[sic]; Me2NNPh, 204-6° (decomposition); 1-pyrrolidinyl, 220-1°; 1-pyrryl, 211-13°; 3-chloro-1-pyrrolyl, 246-7° (decomposition); (3-isopropylidineamino-6-anilino-2-pyrazinecarbonyl)guanidine, 214-16° (decomposition);

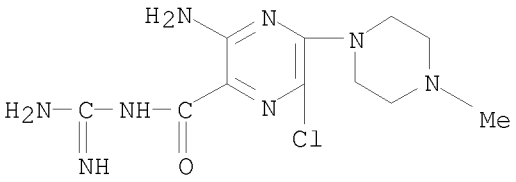
(3-acetoamido-6-methylthio-2-pyrazinecarbonyl)guanidine, 220-2°; the following I (X = NH2, Y = Cl) (R, R1, m.p., and m.p. HCl salt given): H, HOCH2CH2, -, 228.5-9.5° (decomposition); H, Ph, -, -, [MeSO3H salt m. 272° (decomposition)]; H, PhCH2, 215-16° (decomposition); -; H, p-FC6H4CH2, 216-19.5° (decomposition), -; H, PhCHMe, 153-60° (decomposition), -; H, 2-C10H7CH2, 243.5-5.5° (decomposition), -; H, 3-pyridylmethyl, 280.5-3.5° (decomposition), -; H, p-MeC6H4CH2, 210-12° (decomposition), -; Me, PhCH2, 274.5° (decomposition), -; H, o-ClC6H4CH2, 220-3° (decomposition), -; H, p-ClC6H4CH2, 204-6° (decomposition), -; H, p-MeOC6H4CH2, 175.5-9.5° (decomposition), -; H, 2,4-Me2C6H3CH2, 220-2° (decomposition), -; H, 2,4-Cl2C6H3CH2, -, 267.5-70.5° (decomposition); H, 3,4-Cl2C6H3CH2, 216-19° (decomposition), -; H, PhClH,CH2, 219-21° (decomposition), -; Me, Me, 240° (decomposition), -, [HCl.H2O salt m. 275° (decomposition)]; H, octahydrol-azocinyl, -, -; Et, Et, 265° (decomposition), -; Bu, Bu, 148-9°, -; (RR1 =) (CH2)4, -, -; (RR1 =) 3-oxapentamethylene, -, -; the following I (R = R1 = Me, Y = Cl) (X and m.p. given): iso-PrNH, 238-40.5°; CH2:CHCH2NH, 213-15°; BuNH, 187.5°; cyclopropylmethylamino, 196-7°; Me2N, 219°; MeEtN, 217-18°; iso-PrMeN, 209-11°; Et2N, 212-14°; I (R = H, R1 = HOCH2CH2, X = iso-PrNH, Y = Cl).HCl.0.5H2O [m. 185-6° (decomposition)], and 1-(3,5-diamino-6-chloro-2-pyrazinecarbonyl)2,3-dimethylguanidine.

IT 1151-35-5P 1506-24-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 1151-35-5 CAPLUS
CN Pyrazinecarboxylic acid, 3-amino-6-chloro-5-(4-methyl-1-piperazinyl)-, methyl ester (7CI, 8CI, 9CI) (CA INDEX NAME)



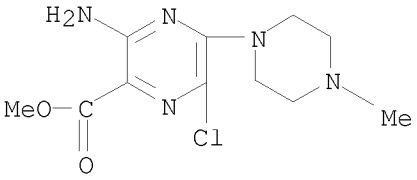
RN 1506-24-7 CAPLUS
CN Pyrazinecarboxamide, 3-amino-N-(aminoiminomethyl)-6-chloro-5-(4-methyl-1-piperazinyl)-, dihydrochloride (9CI) (CA INDEX NAME)



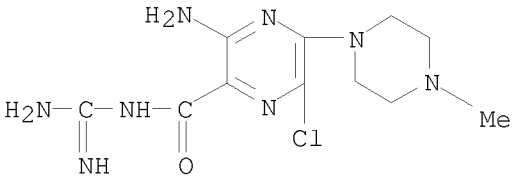
●2 HCl

L5 ANSWER 39 OF 41 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1967:37887 CAPLUS
DOCUMENT NUMBER: 66:37887
ORIGINAL REFERENCE NO.: 66:7227a,7230a
TITLE: Pyrazine diuretics. II. N-amidino-3-amino-5-

substituted 6-halopyrazinecarboxamides
AUTHOR(S): Cragoe, Edward J., Jr.; Woltersdorf, Otto W., Jr.; Bicking, John B.; Kwong, Sara F.; Jones, James Holden
CORPORATE SOURCE: Div. of Merck and Co., Inc., Merck Sharp and Dohme Res. Labs., West Point, PA, USA
SOURCE: Journal of Medicinal Chemistry (1967), 10(1), 66-75
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 66:37887
GI For diagram(s), see printed CA Issue.
AB The synthesis of a series of N-amidino-3-amino-5-substituted-6-halopyrazinecarboxamides (I) is described In rats and dogs, these compds. cause diuresis and saluresis while K excretion is unaffected or repressed Compds. with a variety of 5 substituents including hydroxy, alkoxy, mercapto, alkylmercapto, amino, and substitute amino were prepared The latter 2 tupes embrace compds. with the highest activity. Several routes for the synthesis of Me 3-amino-5,6-dichloropyrazinoate, a key intermediate, are presented. 23 references.
IT 1151-35-5P 1506-24-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 1151-35-5 CAPLUS
CN Pyrazinecarboxylic acid, 3-amino-6-chloro-5-(4-methyl-1-piperazinyl)-, methyl ester (7CI, 8CI, 9CI) (CA INDEX NAME)



RN 1506-24-7 CAPLUS
CN Pyrazinecarboxamide, 3-amino-N-(aminoiminomethyl)-6-chloro-5-(4-methyl-1-piperazinyl)-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

L5 ANSWER 40 OF 41 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1965:82636 CAPLUS
DOCUMENT NUMBER: 62:82636
ORIGINAL REFERENCE NO.: 62:14698f-h,14699a-h,14700a-h,14701a-h,14702a-b
TITLE: Substituted guanidines
INVENTOR(S): Cragoe, Edward J., Jr.
PATENT ASSIGNEE(S): Merck & Co., Inc.
SOURCE: 99 pp.
DOCUMENT TYPE: Patent

LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
BE 639386		19640430	BE	
PRIORITY APPLN. INFO.:			US	19621030

GI For diagram(s), see printed CA Issue.

AB A suspension of 765 g. Me 3-aminopyrazinecarboxylate in 5 l. C6H6 was treated with 1.99 l. SO2Cl2, refluxed for 5 hrs., and left overnight at room temperature to give 888 g. crude Me 3-amino-5,6-dichloropyrazinecarboxylate (I), m. 233-4°. Into a solution of 100 g. I in 1 l. dry Me2SO dry NH3 was passed under stirring at 65-70° for 45 min., then at 10° for 1.25 hrs. to give 82.5 g. Me 3,5-diamino-6-chloropyrazinecarboxylate (II), m. 212-13°. A mixture of 14.2 g. II, 9 g. Pd-C, 4 g. MgO, and 250 ml. MeOH was shaken under H for 18 hrs. at room temperature to give Me 3,5-diaminopyrazinecarboxylate (III), m. 252-4° (decomposition) (iso-PrOH). Bromination of a suspension of 2 g. III in 25 ml. AcOH at 50° with 2.1 g. Br in 10 ml. AcOH gave 1.2 g. Me 3,5-diamino-6-bromopyrazinecarboxylate (IV), m. 217-19°. Hg(OAc)2 (3.2 g.) and a solution of 2.5 g. iodine in 20 ml. warm dioxane was added rapidly to a suspension of 1.7 g. III in 30 ml. H2O at 70°, the mixture heated for 5 min., cooled to room temperature, and treated with 50 ml. 15% KI solution precipitated 1.2 g. Me 3,5-di-amino-6-iodopyrazinecarboxylate, m. 200-2°. I (11.1 g.), 500 ml. iso-PrOH, 14.4 g. PhNH2, and 12.8 g. PhNH2.HCl was refluxed 24 hrs. under stirring to give 10 g. Me 3-amino-5-anilino-6-chloropyrazinecarboxylate, m. 171.5-73° (iso-PrOH). Similarly were prepared Me 3-amino-5-(p-chloroanilino)-6-chloropyrazinecarboxylate, m. 207-8° (MeCN), and Me 3-amino-5-dimethylamino-6-chloropyrazinecarboxylate (V), m. 145.5-6.5° (MeOH). A solution of 10 g. MeSH in 17 ml. 20% NaOH and 100 ml. MeOH was added to a boiling mixture of 17.7 g. I and 1 l. MeOH and refluxed 15 min. to precipitate 12 g. Me 3-amino-5-methylthio-6-chloropyrazinecarboxylate (VI), m. 212-16° (MeOH). VI (23.4 g.), 35 ml. 30% H2O2, and 300 ml. AcOH was stirred 18 hrs. at room temperature to give 18.5 g. the 5-methylsulfinyl analog (VII), m. 237.5-40.5° (decomposition) (MeOH-AcOEt-HCONH2). Hydrolysis of 7.5 g. VII in 75 ml. AcOH and 12 ml. H2O on a steam bath for 3 hrs. produced 3.7 g. Me 3-amino-5-hydroxy-6-chloropyrazinecarboxylate (VIII), m. .apprx.245° (decomposition) (HCONH2-EtOH). Hydrogenation of VIII with Pd-C and MgO at room temperature resulted in Me 3-amino-5-hydroxypyrazinecarboxylate, decompose 220-60°. Also were prepared Me 3-amino-5-dimethyl-aminopyrazinecarboxylate, m. 242.5-3.5°, Me 3,5-diaminopyrazinecarboxylate, m. 252-4° (decomposition), and Me 3-amino-5-methoxypyrazinecarboxylate, m. 205.5-7.5°. A mixture of 8.9 g. I and 20 ml. PhCH2NH2 was heated on a steam bath for 30 sec. to give 7.5 g. Me 3-amino-5-benzylamino-6-chloropyrazinecarboxylate (IX), m. 157-8° (MeOH). Hydrogenation of IX yielded Me 3-amino-5-benzylaminopyrazinecarboxylate, m. 189.5-91.5°. Treatment of 1.1 g. I with MeONa in 200 ml. boiling absolute MeOH produced 1 g. Me 3-amino-5-methoxy-6-chloropyrazinecarboxylate, m. 255-7° (MeCN). Na2S (9.6 g.) and 10 g. S was refluxed in 80 ml. absolute EtOH. Addition of 8.9 g. I at 25° and stirring for 1 hr. gave 7.8 g. Me 3-amino-5-mercapto-6-chloropyrazinecarboxylate, m. 207-8° (decomposition). To a refluxing solution of 4.44 g. I in 300 mil EtOH was added guanidine (from 1.98 g. guanidine-HCl) in 50 ml. absolute EtOH in 15 min. and the mixture refluxed 0.5 hr. to give 3.1 g. Me 3-amino-5-ethoxy-6-

chloropyrazinecarboxylate, m. 123-5° (iso-PrOH). 3-Amino-6-methylpyrazinoylamide (31 g.) was heated 10 min. with 320 ml. 10% NaOH. The resulting Na salt of the acid (97 g.) was methylated with 77 g. Me2SO4 in 700 ml. MeOH 19 hrs. at room temperature to give 18 g. Me 3-amino-6-methylpyrazinecarboxylate (X), m. 138.5-40.5° (C6H6). Chlorination of 9.2 g. X with 65 ml. SO2Cl2 under cooling produced 4.4 g. Me 3-amino-5-chloro-6-methylpyrazinecarboxylate, m. 108.5-10.5° (C6H6-cyclohexane). A mixture of 30 g. 3-amino-5-methylpyrazinecarboxylic acid and a solution of 30% HCl in 650 ml. MeOH was stirred 42 hrs. at room temperature to give 15.4 g. Me 3-amino-5-methylpyrazinecarboxylate (XI), m. 165-7° (H2O). A solution of 4.18 g. Br in 3 ml. AcOH was added to a solution of 4.2 g. XI in 15 ml. AcOH in 20 min. to produce 3.6 g. Me 3-amino-5-methyl-6-bromopyrazinecarboxylate, m. 179-81°. Aminomalonamidamidine-2HCl (52.5 g.) was added to an ice-cooled solution of 28.8 g. ethylglyoxal in 450 ml. H2O. The mixture was made alkaline with .apprx.65 ml. concentrated NH4OH and left 20 hrs. at room temperature to precipitate 17.5 g. 3-amino-6-ethylpyrazinecarboxamide, m. 165.5-8.5° (iso-PrOH), which was saponified 30 min. on a steam bath with 10% NaOH to give 3-amino-6-ethylpyrazine-carboxylic acid (XII), m. 149-52°. Stirring 14 g. XII in a solution of 33% HCl in 160 ml. MeOH 24 hrs. at room temperature gave 4.3 g. XII Me ester, m. 85-7° (iso-PrOH). Also prepared were 3-amino-6-p-chlorophenylpyrazinecarboxylic acid, m. 207-13°, and its Me ester, m. 181.5-3.5°. To a suspension of 17.9 g. 5,6-diaminouracil in 250 ml. H2O at 60° 14.9 g. cyclohexylgiyoxal-0.5 H2O was added and the mixture heated 1 hr. on a steam bath to give 7.5 g. 7-cyclohexyllumazine (XIII), m. 229-31° (aqueous AcOH). A solution of 18.5 g. XIII and 9 g. NaOH in 90 ml. H2O was heated in an autoclave 17 hrs. at 105° to give 8 g. 3-amino-5-cyclohexylpyrazinecarboxylic acid, m. 182.5-3.5° (aqueous iso-PrOH); Me ester m. 173-4.5°. Similarly were prepared Me 3-amino-6-cyclohexylpyrazinecarboxylate, m. 126.5-28°, Me 3-amino-6-cyclopropylpyrazinecarboxylate, m. 112.5-14.5° (amide m. 185.5-7.5°, free acid m. 169-72°), Me 3-amino-5-phenylpyrazinecarboxylate (XIV), m. 231-2°, and Me 3-amino-6-phenylpyrazinecarboxylate (XV), m. 140-1°. Chlorination of 25.6 g. XV with 90 ml. SO2Cl2 1.5 hrs. at room temperature gave Me 3-amino 5-chloro-6-phenylpyrazinecarboxylate, m. 187.5-91.5° (AcOH). Bromination of 10.5 g. XIV in 700 ml. AcOH with 11.2 g. Br 21 hrs. at 85° gave 10.5 g. Me 3-amino-5-phenyl-6-bromopyrazinecarboxylate, m. 217-21° (AcOH). To a suspension of 103.59 g. 4,5-diamino-2,6-dihydroxypyrimidine in 1500 ml. H2O and 500 ml. concentrated NH4OH at 60° 103.71 g. 1-phenyl-1,2-propanedione was added and the mixture heated at 90° under vigorous stirring to give 82.4 g. 6(or 7)-methyl-7(or 6)-phenyllumazine, m. 281.5-2.5° (AcOH), and 32 g. 6(or 7)-phenyl-7(or 6)-methyllumazine (XVI), m. 254.5-5.5°. Saponification of XVI with 8% NaOH in an autoclave 3.5 hrs. at 170° gave 3-amino-5(or 6)-phenyl-6(or 5)-methylpyrazinecarboxylic acid, m. 193.5-4.5°; Me ester m. 163-4° (MeOH). Similarly were prepared 3-amino-5(or 6)-methyl-6(or 5)-phenylpyrazine carboxylic acid, m. 155-6°; Me ester m. 162.5-3.5° (MeOH). Me 3-amino-6-phenylpyrazinecarboxylate was chlorinated with SO2Cl2 to give Me 3-amino-5-chloro-6-phenylpyrazinecarboxylate, m. 187.5-90.5° (AcOH), and subsequently treated with Me2NH in MeOH to give Me 3-amino-5-dimethylamino-6-phenylpyrazinecarboxylate, m. 167.5-9.5° (MeOH). To 750 ml. AcOH and 3180 ml. H2O at 38°, 90 g. Me 3-aminopyrazinecarboxylate was added and Cl passed through in 25 min. to give Me 3-amino-6-chloropyrazinecarboxylate (XVII) m. 142° (decomposition) (H2O). A solution of 18.8 g. XVII, 15 g. PhNH2, and 2.5 ml. concentrated HCl in 150 ml. Me2CO was refluxed 16 hrs. to give 7.4 g. Me 3-isopropylideneamino-6-anilinopyrazinecarboxylate, m. 195.5-7.5° (iso-PrOH). A mixture of 9.3 g. 3-amino-5,6,7,8-tetrahydroquinoxaline-2-carboxylic acid and 230 ml.

absolute MeOH of 10° was treated with 30 ml. concentrated H_2SO_4 in 1 hr. and left 24 hrs. at room temperature to give 1.6 g. the Me ester, m. 154-5° (1:5 MeOH-H_2O). A solution of 60 g. 4-chloro-o-phenylenediamine in 60 ml. H_2O and 50 ml. 12N HCl was treated with a solution of 61.44 g. alloxan-H_2O in 100 ml. H_2O and stirred 1 hr. at 90° to give a precipitate of 78.4 g. 8-chloroalloxazine, m. 365-6° and 40.36 g. 7-chloro-alloxazine, (XVIII) m. 380° (Me_2SO). A mixture of 44.2 g. XVIII and 190 ml. concentrated NH_4OH was heated in an autoclave 10 hrs. at 165° to give 27.2% 3 amino-7-chloroquinoxalin-2-carboxylic acid, m. 191-2° (decomposition); Me ester m. 224.5-5.5° (MeCN). Also prepared are the following XIX (R, R1, % yield, and m.p. given): Me, H, 88, 221-2°; Et, H, 89, 149-50°; Pr, H, 75, 138-40°; iso-Pr, H, 70, 125.5-6.5°; CH_2:$CHCH_2$, H, 69, 105-6.5°; Bu, H, 91, 140-2°; sec-Bu, H, 75, 106-8°; iso-Bu, H, 51, 113.5-15.5°; tert-Bu, H, 38, 98-108°; Am, H, 72, 100.5-2.5°; MePrCH, H, --, --; Et_2CH, H, --, --; C_6H_{13}, H, 70, 72.5-5.5°; cyclopropylnethyl, H, 78, 132-3° cyclopropyl, H, 98, 167-9°; cyclopentyl, H, 93, 119.5-21.5°; $PhCH_2$, H, 64, 157-8°; p-$MeC_6H_4CH_2$, H, 66, 112.5-14.5°; o-$FC_6H_4CH_2$, H, 84, 171-4°; p-$ClC_6H_4CH_2$, H, 93, 136-7°; $PhCH_2CH_2$, H, 59, 115-19°; CF_3CH_2, H, 97, 153-4° $CF_3CH_2CH_2$, H, 76, 124.5-5.5°; $HOCH_2CH_2$, H, 100, 155-7°; $HOCH_2(CHOH)_4CH_2$, H, 60, 172-5°; $NH_2CH_2CH_2$, H, 96, 265°; $Me_2NCH_2CH_2$, H, 40, 257°; 4-pyridylmethyl, H, 69, 95-7°; 2-furylmethyl, H, 81, 148-9°; Me, Et, 73, 102-4°; Me, Pr, 58, 83.5-5.5°; Me, iso-Pr, 78, 75.5-7.5°; Me, CH_2:$CHCH_2$, 70, 90.5-92°; Me, Bu, 74, 59.5-61.5°; Et, Et, 54, 99-101°; Et, Pr, --, --; Et, iso-Pr, --, --; Et, CH_2:$CHCH_2$, --, --; Et, Bu, 91, 77.5-9.5°; Pr, Bu,--, --; Pr, Pr, 66, 68.5-71.5°; (NRR1 =) pyrrolidino, 95, 168-71°; (NRR1 =) 1 (hexahydroazepinyl), 75, 109-11°; (NRR1 =) N'-Methylpiperazino, 88, 186-8°; Me, NH_2, 67, 136.5-38°

Guanidine-HCl (XX) (26.3 g.) was added to a solution of MeONa (5.75 g. Na in 150 ml. absolute MeOH), the precipitated NaCl filtered off, and the filtrate concentrated to 30 ml. After addition of 11.5 g. V the mixture was boiled 1 min., then maintained 1 hr. at room temperature to give 93% (3-amino-5-dimethylamino-6-chloropyrazinecarbonyl) guanidine (XXa), m. 216-17°; HCl salt m. 298° (decomposition). Similarly were prepared (3,5-diamino-6-bromopyrazin-carbonyl)guanidine, m. 232.5-5.5° (decomposition), (3,5-diamino-6-iodopyrazinecarbonyl)guanidine-HCl, m. 273-4° (decomposition) and (3-isopropylideneamino-6-anilinopyrazinecarbonyl)guanidine, m. 214-16° (decomposition). To a solution of 920 mg. Na in 50 ml. absolute iso-PrOH 3.85 g. XX was added and the NaCl filtered off. Adding 4.4 g. I and refluxing the mixture 15 min. gave (3-amino-5,6-dichloropyrazinecarbonyl)guanidine HCl salt (XXb) m. 259-61°. The solution of XXb in 5 ml. HCONMe2 was treated with 1 ml. 25% aqueous Me_2NH 1 hr. on a steam bath to give XXa. Reaction of 11.1 g. I with 55 ml. $Me_2NCH_2CH_2OH$ 20 min. on a steam bath gave 9.5 g. Me 3-amino-5-(2-dimethylamino-ethoxy)-6-chloropyrazinecarboxylate (XXI), m. 134.5-6.5° (C_6H_6-cyclohexane). To 20 g. XX in iso-PrONa (4 g. Na in 100 ml. iso-PrOH) 9.4 g. XXI was added and the mixture heated 30 min. on a steam bath to give 2.5 g. (3-amino-5-guanidino-6-chloropyrazinecarbonyl)guanidine-2HCl, m. >340°. A mixture of 2 1. concentrated NH_4OH and 300 g. XVIII was stirred 16 hrs. at room temperature to give 260 g. 3-amino-6-chloropyrazinecarboxamide (XXII), m. 227-30°. $HC(OEt)_3$ (200 ml.) and 33 g. XXII refluxed in 200 ml. Ac_2O 1.5 hrs. gave 20 g. 4-hydroxy-6-chloropteridine (XXIII), m. 268-70° (decomposition) (iso-PrOH). A solution of 5.5 g. XXIII and 4.4 g. $PhCH_2SH$ in 100 ml. 4% NaOH was heated 30 min. on a steam bath to give 5.5 g. 4-hydroxy-6-benzylthiopteridine, m. 233-5° (aqueous iso-PrOH), which was converted into 3-amino-6-benzylthiopyrazinecarboxylic acid (XXIV), m. 138-9°,

by 8 hrs. hydrolysis with 5% NaOH. XXIV (8.5 g.) in 50 ml. Ac2O was heated 5 hrs. on a steam bath to give 6.6 g. 2-methyl-6-benzylthio-4H-pyrazino[2,3-d][1,3]oxazin-4-one (XXV), m. 116.5-18.5° (C6H6). To 1 g. Na in 30 ml. iso-PrOH 5 g. XX and 3.4 g. XXV were added to give, after 1 hr. at room temperature, 1.1 g. (3-amino-6-benzylthiopyrazinecarbonyl-guanidine, m. 171-3° (decomposition). Similarly were prepared 4-hydroxy-6-methylthiopteridine, m. 289.5-91.5° (aqueous iso-PrOH), 3-amino-6-methylthiopyrazinecarboxylic acid (XXVI), m. 182-4° (decomposition) (AcOEt), 2-methyl-6-methylthio-4H-pyrazino[2,3-d][1,3]oxazin-4-one, m. 189-91° (C6H6), and 3-acetamido-6-methylthiopyrazinecarbonyl)guanidine (XXVII), m. 220-2°. Addition of HCl to XXVII in H2O gave 86% (3-amino-6-methyl-thiopyrazinecarbonyl)guanidine, m. 203-5°. A solution of 0.92 g. XXVI in 15 ml. 2.5% NaOH was treated with 1.05 g. KMnO4 in 35 ml. H2O to give 0.5 g. 3-amino-6-methylsulfonylpyrazine-carboxylic acid, m. 239-42° (decomposition) (iso-PrOH), which gave, after 5 hrs. heating in Ac2O, 2-methyl-6-methylsulfonyl-4H-pyrazino[2,3-d][1,3]oxazin4-one, m. 214-16° (Me2CO), transformed into 27% 3-amino-6-methylsulfonylpyrazinecarbonyl)guanidine, m. 224-6° (decomposition) (iso-PrOH). Similarly are prepared the following XXVIIa (R, R1, % yield, and m.p. given): H, H, 93, 240.5-1.5°; 293.5° (HCl salt); Me, H, 89, 238-9°; Et, H, 63, 217-18°; Pr, H, 93,221-2°; iso-Pr, H, 75, 215°; CH2:CHCH2, H, 84, 213-14°; Bu, H, 65, 219.5°; Me-ETCH, H, 74, 208-9°; iso-Bu, H, 76, 221°; tert-Bu, H, 84, 222-3°; Am, H, 70, 215-16°; MePrCH, H, 89, 186.5-8.5°; Et2CH, H, 82, 209-11°; C6H13, H, 100, 194.5-6.5°; cyclopropylmethyl, H, 95, 220-1°; cyclopropyl, H, 85, 213-15°; cyclopentyl, H 65, 219-20°; PhCH2, H, 44, 206-9°; p-MeC6H4CH2, H, 57, 216-17°; o-FC6H4CH2, H, 100, 206-8°;. p-ClC6H4CH2, H, 96, 225-6°; PhCH2CH2, H, 57, 199-202°; CF3CH2, H, 77, 232-3°; CF3CH2CH2, H, 65, 221-2.5°; HO-CH2CH2, H, 63, 272-3°; HOCH2(CHOH)4CH2, H, 68, 223-4°; NH2CH2CH2, H, 68, 311°; Me2NCH2CH2, H, 98, 192.4-4.5°; 4-pyridylmethyl, H, 64, 239-40°; o-furylmethyl, H, 92, 217-18°; Ph, H, 95, 246.5-8.5°; p-ClC6H4, H, 95, 276-8°; Me, Et, 92, 229-30°; Me, Pr, 97, 214-15°; Me, iso-Pr, 70, 207-8°; Me, CH2:CHCH2, 95, 207-8°; Me, Bu, 95, 208-9°; Et, Et, 75, 215°; Et, Pr, 92, 224-5°; Et, iso-Pr, 75, 207-8°; Et, CH2:CHCH2, 92, 208-9°; Et, Bu, 98, 200.5-1.5°; Pr, Pr, 100, 221-2°; Pr, Bu, 84, 215-17°; (NRR1 =) pyrrolidino, 90, 244.5-5.5°; (NRR1 =) 1-hexahydroazepinyl, 49, 224-5°; (NRR1 =) N-methylpiperazino, 74, 299-300°; Me, NH2, 92, 234°.
Also prepared are the following XXVIIb (X, Y, % yield, and m.p. base and m.p. HCl salt given): H, HO, 10, >310° (decomposition); H, NH2, 8, 286-8° (decomposition), --; H, NMe2, 45, 224-5° (decomposition), --; H, MeO, 52, --, 229-30° (decomposition); H, PhCH2NH, 56, --, 231-7° (decomposition); Cl, MeO, 90, --, 257°; Cl, MeS, 100, 234.5-6.5°, --; Cl, HO, 24, --, >300° (decomposition); Cl, SH, 100, 236.5° --; Cl, EtO, 81, 215-16° --; Cl, Cl, 72, --, 259-61°; Me, H, 87, 218-19 (decomposition), --; Me, Me2N, 42, --, 262° (decomposition) (di-HCl); H, Me, 13,210° (decomposition), --; Me, Me, 38, 245° (decomposition), --; Br, Me, 35, 288° (decomposition), --; Et, H, 53, 207.5-9.5° (decomposition), --; H, cyclohexyl, 71, 221-2° (decomposition), --; cycloheptyl, H, 61, 228-30° (decomposition), --; cyclopropyl, H, 61, 196.5-99° (decomposition), --; H, Ph, 51, 224-6° (decomposition); Ph, H, 34, 194.5-5.5° (decomposition), --; Ph, Ph, 87, 234.5-5.5°, -; Ph, Cl, 69, 214-16° (decomposition), --; Br, Ph, 66, 234-6° (decomposition), --; p-ClC6H4, H, 70, 282-5° (decomposition), --; Me (or Ph), Ph (or Me), 77, 212-13° (decomposition), --; Ph (or Me), Me (or Ph) 90, 218-19° (decomposition), --; Ph, Me2N, 40, 205-6° (decomposition), --; (XY =)(CH2)4, 29,

220-1°, --; (XY =) CH:CHCH:CH, 56, 211-13°, --; (XY =) HC:CClCH:CH, 70, 246-7° (decomposition), --. A solution of 13.9 g. 2-methyl-2-pseudothiuronium sulfate (XXVIII) and 9.2 g. H2NCH2CH2OH in 40 ml. H2O was heated 20 min. to give 12.5 g. (2-hydroxyethyl)guanidine sulfate, m. 127.5-35.5°, which was added to a solution of 2g. Na in 25 ml. MeOH, MeOH distilled, and the residue treated with 4.1 g. II 5 min. on steam bath to give 1.2 g. 1-(3,5-diamino-6-chloropyrazinoyl)-3-(2-hydroxyethyl)guanidine-HCl, m. 228.5-9.5° (aqueous iso-PrOH). 1-(3-Amino-5-isopropylamino-6-chloropyrazinoyl)-3-(2-hydroxyethyl)guanidine-HCl.0.5H2O, m. 185-6° (decomposition), was prepared from Me 3-amino-5-isopropylamino-6-chloropyrazinecarboxylate. A mixture of 6.1 g. II, 6.8 g. phenylguanidine, and 3 ml. iso-PrOH was heated 6 hrs. to give 1-(3.5-diamino-6-chloropyrazinoyl)-3-phenylguanidine, isolated as the MeSO3H salt, m. 272° (decomposition) (H2O). Ph-CH2NH2 (80.3 g.) and 69.5 g. XXVIII in 200 ml. H2O kept 18 hrs. at room temperature gave benzylguanidine sulfate, which was converted into the HCl salt (XXIX) (51.5 g.), m. 175-8° (aqueous EtOH), by treating its aqueous solution with aqueous BaCl2. To a solution of 1 g. Na in 30 ml. iso-PrOH 9.3 g. XXIX was added and half the volume distilled Addition of 2 g. II and heating the mixture 15 min. yielded 1 g. 1-(3,5-diamino-6-chloropyrazinoyl)-3-benzylguanidine, m. 215-16° (decomposition) (aqueous iso-PrOH). With the appropriate starting materials the following 3-substituted 1-(3,5-diamino-6-chloropyrazinoyl)guanidines were prepared [3-substituent and m.p. (decomposition) given]: p-fluorobenzyl 216-19.5°; α-methylbenzyl 153-60°; 3-pyridylmethyl, 280.5-3.5°; 2-naphthylmethyl 243.5-5.5°. Also prepared were the following RR1-NC(:NH)NH2.HCl (R, R1, % yield, and m.p. given): p-Me-C6H4CH2 H, 28, 153-5°; o-ClC6H4CH2, Me, 32, 122.5-5.5°; PhCH2, H, 71, 131-6°; p-ClC6H4CH2, H, 55, 162.5-4.5°; p-MeOC6H4CH2, H, 69, 132-7°; 2,4-Me2C6H3CH2, H, 52, 105-15°; 2,4-Cl2C6H3CH2, H, 67, 145-8°; 3,4-Cl2C6H4CH2, H, 77, 155-7°; PhCH2CH2, H, 71, 135-8°.

Also prepared were the following XXIXa [R, R1, % yield, and m.p. (decomposition)given]: p-MeC6H4CH2, H, 27, 210-12°; PhCH2, Me, 35, 274.5° (HCl salt); o-ClC6H4CH2, H, 39, 220-3°; p-ClC6H4CH2, H, 46, 204-6° p-MeOC6H4CH2, H, 27, 175.5-9.5°; 2,4-Me2C6H3CH2 H, 59, 220-2°; 2,4-Cl2C6H3CH2, H, 30, 267.5-70.5° (HCl salt); 3,4-Cl2C6H3CH2, H, 47, 216-19°; PhCH2CH2, H, 46, 219-21.5°. To a solution of 2.3 g. Na in 200 ml. absolute MeOH 15 g. dimethyl-guanidine sulfate was added, the mixture refluxed 1 hr. and cooled, Na2SO4 filtered off, the solution concd, to 30 ml., 10.15 g. II added, and the mixture heated 30 min. and kept 1 hr. at room temperature to give 3.6 g. 1-(3,5-diamino-6-chloropyrazinoyl)-3,3-dimethyl-guanidine (XXX), decomposing at 240° HCl salt m. 275° (decomposition). To a solution of 36.57 g. Et2NH in 100 ml. H2O and 41 ml. concentrated HCl adjusted, with 3.66 g. Et2NH to pH 9.2 a solution of 50% aqueous cyanamide (65.16 g.) was added dropwise at 100° in 4 hrs. After refluxing 1 hr. and standing over night at room temperature the mixture was treated with 50 ml. of 40% NaOH and CO2 passed through under cooling to give 1,1-diethylguanidine, isolated as the HCl salt (XXXI) (35 g.), m. 147-9°. Similarly, 1,1-dibutylguanidine-HCl (XXXII), m. 104.5-106° (H2O), was obtained in 86% yield. The following compds. were also prepared: 88.6% 1 - (3,5-diamino-6-chloropyrazinoyl)-3,3-diethylguanidine, m. 265° (decomposition), from II and XXXI and 72% 1-(3,5-diamino-6-chloropyrazinoyl)-3,3-dibutylguanidine, m. 148-9° (iso-PrOH), from II and XXXII.

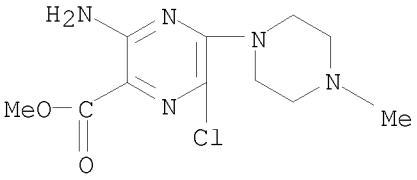
Also prepared were the following XXXIII (R, R1, % yield, and m.p. given): iso-Pr, H, 35, 238.5-40°; CH2:CHCH2, H, 39, 215°; Bu, H, 17, 187.5°; cyclopropylmethyl, H, 3, 196-7°; Me, Me, 69,

219°; Me, Et, 49, 218°; Me, iso-Pr, 61, 209-11°; Et, Et, 40,214°. The compds. are effective in the treatment of abnormal electrolyte excretion.

IT 1151-35-5P, Pyrazinecarboxylic acid, 3-amino-6-chloro-5-(4-methyl-1-piperazinyl)-, methyl ester 1506-24-7P, Pyrazinecarboxamide, N-amidino-3-amino-6-chloro-5-(4-methyl-1-piperazinyl)-, dihydrochloride
RL: PREP (Preparation)
(preparation of)

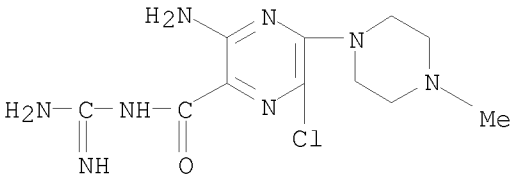
RN 1151-35-5 CAPLUS

CN Pyrazinecarboxylic acid, 3-amino-6-chloro-5-(4-methyl-1-piperazinyl)-, methyl ester (7CI, 8CI, 9CI) (CA INDEX NAME)



RN 1506-24-7 CAPLUS

CN Pyrazinecarboxamide, 3-amino-N-(aminoiminomethyl)-6-chloro-5-(4-methyl-1-piperazinyl)-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

L5 ANSWER 41 OF 41 CAPLUS COPYRIGHT 2008 ACS on STN

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TITLE: Substituted aminopyrazinylcarboxamidoguanidines

INVENTOR(S): Cragoe, Edward J., Jr.

PATENT ASSIGNEE(S): Merck & Co., Inc.

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BE 639393		19640430	BE	
NL 299929			NL	
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GI For diagram(s), see printed CA Issue.

AB I were prepared and showed natriuretic activity. Me 3-amino-pyrazine-2-carboxylate (II) (90 g.) in 3180 cc. H2O and 750 cc. AcOH treated with stirring below 40° during 25 min. with .apprx.140 g. Cl yielded Me 3-chloroamino-6-chloropyrazine-2-carboxylate (III), m. 142° (AcOH);

crude III stirred 0.5 hr. at 25° with 150 g. NaHSO3 in 900 cc. H2O yielded 60 g. 6-Cl derivative (IV) of II, m. 159-61°. H2NC(:NH)NHNH2.H2CO3 (V.H2CO3) (275 g.) in 1500 cc. H2O treated at 50-60° during 0.5 hr. with 300 cc. 12.2N HCl gave 211 g. V.HCl, m. 160-2° (absolute EtOH). V.HCl (120 g.) in 2 l. boiling absolute EtOH treated with stirring with 23 g. Na in 500 cc. absolute EtOH and then at room temperature with 100 g. powdered IV, and the mixture concentrated in vacuo at 25-35° to 600 cc. during 6 hrs. and kept 20 hrs. under N yielded 58 g. I (R = Cl, R1 = R2 = R3 = R4 = H) (VI), which stirred 15 min. on a steam bath with 200 cc. 6N HCl yielded 24 g. VI.HCl, m. 277-8° (7:3 iso-PrOH-H2O). VI.HCl (2 g.) in 10 cc. hot H2O with 3.5 g. maleic anhydride in 3 cc. H2O gave the acid maleate of VI, m. 210-12° (decomposition) (H2O). Similarly were prepared 2VI.H2SO4.H2O, m. 209-11° (decomposition), and 3VI.H3PO4.H2O, m. 280-80.5° (decomposition). IV (94 g.) in 2.2 l. absolute EtOH refluxed 2 hrs. with 32 g. N2H4 yielded 94 g. 3-amino-6-chloropyrazine-2-carbohydrazide (VII), m. 218-20° (EtOH). VII (5 g.) in 50 cc. Me2SO heated 20 hrs. on a steam bath with 11 g. MeSC(:NH)NH2.HI (VIII) and 2.65 g. NaOMe in Me2SO under N, treated again with 11 g. VIII and 2.65 g. NaOMe, and heated 24 hrs. under N and the product treated with 10% HCl yielded 3.3 g. VI.HCl, m. 277-8° (decomposition). VII (25 g.) in 400 cc. absolute EtOH refluxed 5 hrs. with 44 cc. 10% HCl and 6.8 g. H2NCN in 25 cc. absolute EtOH, treated again with 6.8 g. H2NCN and 11 cc. 36% HCl, and refluxed 15 hrs. yielded 23.5 g. VI.HCl. IV (150 g.) heated 15 hrs. with 800 cc. 2.5N NaOH on a steam bath gave 127 g. 3-amino-6-chloropyrazine-2-carboxylic acid (IX), m. 178.5-9.5° (EtOH). IX (127 g.) in 550 cc. Ac2O stirred 1 hr. on a steam bath yielded 6-chloro-2-methyl-4-pyrazino[2,3-d]-1,3-oxazin-4-one (X), m. 158-60° (decomposition) (AcOEt). V, from 5 g. V.HCl, in 100 cc. EtOH with 6 g. X in 125 cc. AcOEt yielded 1.2 g. I (R = Cl, R2 = Ac, R1 = R4 = R3 = H), m. 204-6° (decomposition), which heated 15 min. on a steam bath with 150 cc. 5% HCl, and adjusted at room temperature to pH 12 with 10% aqueous NaOH gave 2 g. VI, m. 333-4° (decomposition). VI with 10% HCl yielded VI.HCl. 3-Br derivative (12 g.) of II and V gave in the usual manner 1.9 g. I.HCl (R = Br, R1 = R2 = R3 = R4 = H), m. 270-1° (decomposition) (7:3 iso-PrOH-H2O). II (30.6 g.) in 500 cc. H2O and 39.8 g. Hg(OAc)2 treated with stirring on a steam bath with 50.8 g. iodine in 250 cc. hot dioxane, refluxed 40 min., and stirred into 600 cc. 15% aqueous KI yielded 13.5 g. 6-iodo derivative (XI) of II, m. 200-2° (AcOH). XI (5 g.) with V gave 1.1 g. HCl salt of I (R = I, R1 = R2 = R3 = R4 = H), m. 256-7° (decomposition) (7:3 iso-PrOH-H2O). [MeSC(NH2)NHNH2]I (23 g.) in 150 cc. refluxing, absolute EtOH treated during 10 min. with 6.5 g. HOCH2CH2NH2 in portions yielded HOCH2CH2NHC(:NH)NHNH2.HI (XII.HI). IV (10 g.) with XII from 25 g. XII.HI yielded I.HCl (R = Cl, R1 = R2 = R3 = H, R4 = HOCH2CH2), m. 243-4° (decomposition) (iso-PrOH-H2O). Me2NCSNH2 (18 g.) in 175 cc. hot, absolute EtOH treated during 15 min. with stirring with 23 g. PhCH2Cl in portions and refluxed 1 hr. gave 35.5 g. PhCH2SC(:NH)NMe2.HCl (XIII.HCl), m. 171-2.5°. XIII.HCl (23 g.) in 100 cc. Me2SO and NaOMe from 2.3 g. Na heated 16 hrs. on a steam bath with 9.4 g. VII, and the product treated with 200 cc. hot 2% HCl yielded 3.7 g. I.HCl (R = Cl, R1 = R2 = H, R3 = R4 = Me). Similarly were prepared the I.HCl (R3 = H) listed in the table. CF3COCHBr2 (97.83 g.), 98.6 g. AcONa.-3H2O, and 30.5 cc. H2O refluxed 25 min. with stirring, treated under N at 0° with 68.51 g. H2NCH[C(:NH)NH2]2.2HCl, adjusted with concentrated NH4OH to pH 8-9, and stirred 20 hrs. under N yielded 20 g. yellow XV (R = CF3 or H, R1 = H or CF3), X = CONH2) (XVI), m. 195-6° (AcOH). XVI (18.55 g.) and 740 cc. 5% aqueous NaOH refluxed 10 min. with stirring yielded 17.78 g. XV (R = CF3 or H, R1 = H or CF3, X = CO2H) (XVII), m. 185-6° (decomposition) (MePh). XVII (16.57 g.) stirred 19 hrs. at room temperature in 495 g. dry HCl in 1650 cc. MeOH gave XV [R = CF3 or H, R1 = H or CF3), X = CO2Me], m.

195.5-6.5° (MeOH). PhCH2CH2NH2 (6.7 g.) in 15 cc. absolute EtOH refluxed 12 hrs. with 12 g. MeSC(:NH)NHNH2.2HI in 35 cc. absolute EtOH gave MeSH and PhCH2CH2NHC(:NH)NHNH2.HI. II (765 g.) in 5 l. dry C6H6 treated with stirring with 3318 g. SO2Cl2 during 0.5 hr., stirred 1 hr., refluxed 5 hrs., and stirred about 12 hrs. at room temperature gave 888 g. red XV (R = R1 = Cl, X = CO2Me) (XVIII), m. 228-30°, which dissolved in 56 l. hot MeCN and passed at 70-80° through 444 g. C yielded 724 g. pure, yellow XVIII, m. 233-4° (MeCN). XVIII (100 g.) in 1 l. dry Me2CO treated during 45 min. at 65-70° with stirring with dry NH3, cooled to about 10°, treated again 75 min. with dry NH3, and stirred into 2 l. cold H2O yielded 82.5 g. XV (R = Cl, R1 = NH2, X = CO2Me), m. 212-13° (MeCN). XIV (14.2 g.), 9 g. 5% Pd-C, 4 g. MgO, and 250 cc. MeOH hydrogenated 18 hrs. at room temperature and 2.1 atmospheric yielded 10 g. XV (R = H, R1 = NH2, X = CO2Me) (XIX), m. 252-4° (iso-PrOH). XIX (2 g.) in 25 cc. AcOH treated at 50° with 2.1 g. Br in 10 cc. AcOH gave 1.2 g. XV (R = Br, R1 = NH2, X = CO2Me), m. 217-19° (iso-PrOH). XVIII (178 g.) in 1.1 l. iso-PrOH refluxed 1 hr. with 200 g. Me2NH in 2 l. iso-PrOH gave 177.2 g. XV (R = Cl, R1 = Me2N, X = CO2Me), m. 145.5-6.5° (MeOH). Similarly were prepared the following XV (R = Cl, X = CO2Me) (R1, m.p., and % yield given): CH2:CHCH2NH, 105-6.5° (iso-PrOH), 69; iso-PrNH, 125.5-6.5° (iso-PrOH), 70; AmNH, 100.5-2.5° (cyclohexane), 72; cyclopropylmethylamino, 132-3° (iso-PrOH), 78; cyclopropylamino, 167-9° (iso-PrOH), 98; cyclopentylamino, 119.5-21.5° (iso-PrOH), 93; PhCH2NH, 157-8° (MeOH), 64; p-MeC6H4CH2NH, 112.5-14.5° (iso-PrOH), 66; p-ClC6H4CH2NH, 136-7°, 93; CF3CH2NH, 153-4°, 97; HOCH2CH2NH, 155-7° (iso-PrOH), 100; H2NCH2CH2NH, 265° (MeOH), 96; Me2NCH2CH2NH, 257° (MeOH), 40; 4-pyridylmethylamino, 95-7°, 69; 2-furylmethylamino, 148-9° (iso-PrOH), 81; MeEtN, 102-4° (iso-PrOH), 73; CH2:CHCH2NEt, --, --; MeONMe, 144-6° (iso-PrOH), 68; pyrrolidino, 166-71° (iso-PrOH), 95; 1-aza-1-cycloheptyl, 109-11° (iso-PrOH), 75; 4-methylpiperazino, 186-8° (iso-PrOH), 88.

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RL: PREP (Preparation)
(preparation of)

RN 1151-35-5 CAPLUS

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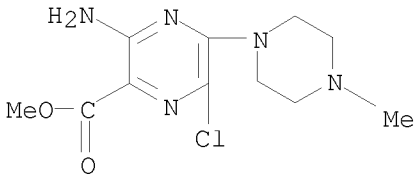

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	169.03	348.44

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-20.80	-20.80

SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 13:10:50 ON 20 MAY 2008